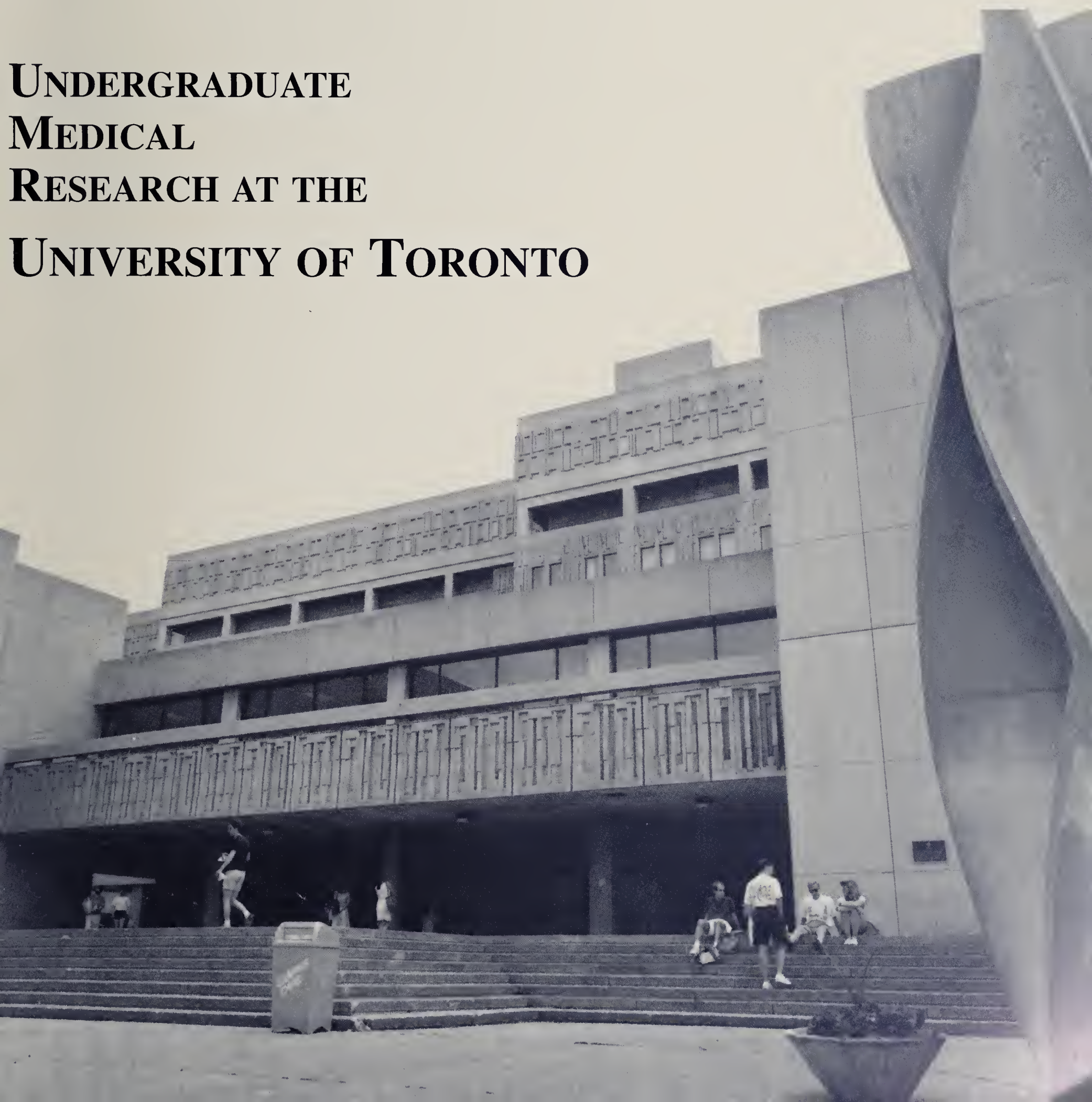
January 1996

University of Toronto

Volume 73, Supplement

Medical Journal

Undergraduate Medical Research at the University of Toronto



University of Toronto

Medical Student Research Day

January 9, 1995

1:00-2:00 pm Visiting Speaker: Dr. Brenda Millner
Medical Sciences Building Room 3153

2:00-4:30 pm Student Poster Presentations and Competition
Medical Sciences Building, Stone Lobby

4:45-5:30 pm Presentations by winners of 1994 Research Day Competition:
Medical Sciences Building Room 3153

Peter Ballyk — *The role of wall mechanics in arterial bypass graft failure.*

Amit Mehta — *Alteration in the normal pattern of cervical spinal cord motion as measured by MRI in selected pathologic states.*

Taufik Valiante — *TBA*

Bradley Wilcox — *Dietary factors in prostate cancer in Japan and Canada.*

5:30 ***Award Presentation and Wine and Cheese Reception***

Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalJan1996uoft

MESSAGE FROM THE DEAN

Welcome to the 10th Annual Medical Student Research Day. This is an important day for the Faculty of Medicine, because it provides an opportunity for our undergraduate medical students to showcase the wide spectrum of research projects they have completed, often during summer fellowships. These projects range from investigations of basic cellular activity to studies of clinical applications in hospitals and community involvement, revealing the many career pathways open to today's medical students.

Medical Student Research Day was first suggested in 1986 by Dr. Michael Pare, who was a second year medical student at the time. The Faculty supported the idea and Dr. Niall Byrne took on the task of organizing the first Research Day in 1986. In time, Dr. Catharine Whiteside got involved and brought in much-needed corporate support from Merck-Frosst and others. Diana Alli (Office of Student Affairs) provides administrative support for the annual event. Together these four individuals are an outstanding organizational team and last year they were honoured with an Aikins Award for developing and co-ordinating the annual event.

Taking a research project from concept to completion provides undergraduates with a stimulating learning experience, giving them the opportunity to discover if they have the self-discipline, dedication and creative thinking required to be a successful investigator. As Dean, I am proud to say that many of our undergraduate medical students do have these qualities. Take a look at their research projects and you will see what I mean. Our Faculty has a great tradition of breakthroughs in medical research and it is my hope that many of the students involved in today's Medical Student Research Day will continue that tradition. Congratulations to all the participants - and many thanks to the faculty members who made this year's event possible.

Arnie Aberman

MESSAGE FROM THE VICE-DEAN, EDUCATION

Welcome to the 10th annual Faculty of Medicine Undergraduate Medical Student Research day. Each year this event provides an opportunity for undergraduate students to display the results of their research. This research highlights the many paths for research from basic molecular biology to clinical outcomes and community health that are open to Medical graduates. Taking a research project from concept to competition gives undergraduates the opportunity to demonstrate that they have the self-discipline, dedication and creativity required of a successful investigator. Their abstracts and posters provide ample evidence of these qualities.

Each summer approximately 100 medical students receive scholarships through the Faculty of Medicine enabling them to work on projects in basic science laboratories and clinical investigative settings. Approximately 40% of the students who apply are funded based on scholarship and merit of the research proposed. They, and the students in the MD-PhD research programme, present their work at Medical Student Research Day. The top-rated students in the categories of basic and clinical research, receive an all-expense paid trip to the Annual Medical Student Research Forum (U.S.A.) in Galveston, Texas, in April, representing our Faculty. The Department of Medicine also supports the top-rated student (in either category), supervised by one of its members, to attend the same meeting.

The undergraduate students in the Division of Biomedical Communications, Department of Surgery, also present their creative work in poster format at Research Day.

Why do students wish to extend their professional training into the realm of biomedical research? There are many reasons including scientific curiosity and extension of previous engagement in research (more than 25% of students now entering medicine at Toronto hold graduate degrees). Many of the students will contribute to scientific papers published in peer-reviewed journals. Some will seek future career development as Clinician-Scientists, by entering graduate or post-graduate research programmes during or after clinical specialty training. The Faculty of Medicine at the University of Toronto is a major focus of basic and clinical investigation in Canada. It is no wonder that our medical students wish to take advantage of this rich learning environment.

The students participating in research day have taken time out of a demanding professional training programme to prepare and present their posters. The challenge for health care professionals engaged in research is to maintain a balance between clinical and investigative responsibilities. The students who participate in Research Day begin to experience this sometimes difficult, yet highly rewarding, duality.

The students and Faculty are indebted to the Medical Student Committee who worked so hard and efficiently in the planning and preparation for Research Day and to Dr. Catherine Whiteside who continues to provide encouragement, and support for the students.

Andrew D. Baines
for the Research Day Coordinating Committee

The Faculty of Medicine gratefully acknowledges support from

Astra Pharma

Glaxo Wellcome

Servier Canada

Merck Frosst

Last year three companies gave their support

Organon Canada

Whitehall Robins

Boehringer Ingelheim

COMMITTEE MEMBERS

Faculty Advisors
Dr. Andrew Baines
Dr. Catharine Whiteside

Students
Sean Bulley, M.Sc. 9T7
Charles Dela Cruz, B.Sc. 9T8
David Hwang , B.Sc. 9T6
Catherine Mason, M.Sc. 9T8
Melinda Anne Musgrave, Ph.D. 9T8
Monique Piersanti, M.Sc. 9T8)
Tom Ransom, M.Sc. 9T8
Ally-Khan Somani, B.Sc. 9T7
Sohail Somani, Ph.D. 9T8

Secretary
Shakilah Merunnisa

EDITORIAL STAFF

Editors-in-Chief
Mark Korman, B.A. 9T8
Mary K. Nagai, Ph.D. 9T8

Treasurer
David Goldstein, B.A. 9T8

Secretary
Joan Caverly

Photography
IMS-Creative Communications

Typesetting and Artwork
Type & Graphics

Printer
Pristine Printers Inc.

PATRONS

The staff of the Journal wish to thank the following patrons for their generous support:

Dr. Sharon M. Abel
Dr. Arnold Aberman
Dr. E.C. Allen
Dr. Douglas Alton
Dr. Kofi Amankwah
Dr. Crawford Anglin
Dr. Sylvia L. Asa
Dr. Mary Jane Ashley
Dr. Marvin L. Auerbach
Dr. Mary Ann Badali
Dr. Michael A. Baker
Dr. Joanne M. Bargman
Dr. Eric J. Barker
Dr. Jack Barkin
Dr. Marshal P. Barkin
Dr. N. Bayer
Dr. Susan Belo
Dr. Sam Berger
Dr. John A. Beswick
Dr. Erin Boynton
Dr. A. Bruce-Robertson
Dr. P.J. Brueckner
Dr. Brian Butler
Dr. David S. Byers
Dr. Lorie Cappe
Dr. Daniel Cattran
Dr. A Cecutti
Dr. Jeff Charendoff
Dr. Pamela Chart
Dr. Davy Cheng
Dr. Albert Cheskes
Dr. Robert J. Chisholm
Dr. Joseph Y. Chu
Dr. Howard M. Clarke
Dr. Eriz A. Cohen
Dr. Vincent P. Collins
Dr. John Connolly
Dr. J.J. Connon
Dr. Paul Cotterill
Dr. Donald Cowan
Dr. John Crawford
Dr. Michael Crump
Dr. E. Laura Cruz
Dr. Derek Davidson
Dr. Helen P. Demshar
Dr. H. Roslyn Devlin
Dr. S.P. Dhiman
Dr. N.E. Diamant
Dr. Bernard M. Dickens
Dr. Sheila Doyle
Dr. James Duffin
Dr. Stuart Z. Dyment
Dr. Gerald Edelist
Dr. John Edmeads
Dr. John F. Edmonds
Dr. S. Epstein
Dr. Inara Ezers
Dr. Duncan Farquaharson
Dr. Christopher Feindel
Dr. Ronald Fenton
Dr. Robert Filler
Dr. Joseph Fisher
Dr. J. Fleming
Dr. Christopher R. Forrest
Dr. W.H. Francombe
Dr. T.J. Freedman
Dr. Arnis Freiberg
Dr. Gordon Froggatt
Dr. Kan Ying Fung
Dr. Steven Gallinger
Dr. A.E.M Geisler
Drs. Richard & Joan Gladstone
Dr. Alan Goldbloom
Dr. David S. Goldbloom
Dr. Barry Goldlist
Dr. Irvin Gollish
Dr. Avrum Gotlieb
Dr. Ian Graham
Dr. Allan E. Gross
Dr. Lawrence Grossman
Dr. Michael L. Guinness
Dr. P. Gullane
Dr. Abraham L. Halpern
Dr. Mary Hannah
Dr. Ian Harrington
Dr. Robert H.A. Haslam
Dr. E. Heathcote
Dr. Dianne Margaret Heritz
Dr. Robert C. Hicks
Dr. Robert Hilliard
Dr. Sophie Hofstader
Dr. Charles Hollenberg
Dr. William J. Horsey
Dr. Robert Howard
Dr. Michael A. Hutcheon
Dr. Paul A. Hwang
Dr. R.H. Hyland
Dr. Masanori Ichise
Dr. Richard J. Inman
Dr. Jonathan Irish
Dr. Jaya Islur
Dr. Andrew James
Dr. Christopher Jamieson
Dr. D. Anna Jarvis
Dr. Michael Jewett
Dr. Margaret Jury
Dr. Gabor P. Kandel
Dr. Armand Keating
Dr. John D. Kempston
Dr. Alexander Kennedy
Dr. Jay S. Keystone
Dr. B.W. Knox
Dr. Stephen Kraft
Dr. Robert Kyle
Dr. C. Lambert
Dr. Richard Lamon
Dr. Bernard Langer
Dr. Brian C. Leong-Poi
Dr. Samuel Librach
Dr. William K. Lindsay
Dr. Frank Lista
Prof. Emeritus S. Liswood
Dr. E. Lo
Dr. Lynn Loach
Dr. Konstanin Loewig
Dr. Ross MacKay
Dr. J. L. Madigan
Dr. James Mahoney
Dr. Leo Mahoney
Dr. O. J. Mandel
Dr. Paul H. Marks
Dr. Jaanus Marley
Dr. Joseph Marotta
Dr. A. Bruce Marshall
Dr. Ray D. Martin
Dr. Robert G. Maunder
Dr. A.W. Maykut
Dr. Steven Mc Cabe
Dr. Dale McCarthy
Dr. Hugh D. McGowan
Dr. N. McKee
Dr. David McNeely
Dr. Rosemary Meier
Dr. D. Mendelssohn
Dr. E. Michel
Dr. A.A. Minor
Dr. David Mock
Dr. Charles Moes
Dr. Robert W. Moore
Dr. Heather Morris
Dr. Rebeka Moscarello
Dr. Richard J. Moulton
Mount Sinai Hospital
(Medical Library)
Dr. Paul Muller
Dr. Martin Myers
Dr. Salim Naqvi
Dr. A. John B. Nazareth
Dr. J.M. Nedzelski
Dr. Richard I. Ogilvie
Dr. Allen B. Okey
Dr. Charles Omole
Dr. Dimitrios Oreopoulos
Otolaryngology Faculty,
Mount Sinai Hospital
Dr. Howard J. Ovens
Dr. Daniel Panisko
Dr. Fred Papsin
Dr. John D. Parker
Dr. Robert Patten
Dr. Thomas A. Patterson
Dr. Charles F. Pearce
Dr. G. Allan Pengelly
Dr. Charles Peniston
Dr. W. J. Peters
Dr. Mel Petersiel
Dr. Anne Phillips
Dr. Eliot Phillipson
Dr. Brian Power
Dr. Kenneth Pritzker
Dr. William J. Prost
Dr. Ronald J. Puley
Dr. Anita Rachlis
Dr. G.L. Ralph
Audrey & Robert Randall
Dr. Joel Raskin
Dr. Donald Redelmeier
Dr. John H. Richard
Dr. Robin Richards
Dr. David Rideout
Dr. Joseph E. Rogers
Dr. Irving E. Rosen
Dr. Frank W. Rosenberg
Dr. Lorne E. Rotstein
Dr. Cheryl Rowe
Dr. R.L. Ruderman
Dr. Donato Ruggiero
Dr. John Rutka
Dr. Fred Saibil
Dr. Michael K. Sarin
Dr. Daniel N. Saunder
Dr. J.G. Scott
Dr. Jerry Shime
Dr. Barry H. Shrott
Dr. Jack Shuber
Dr. K.H. Shumak
Dr. Ivan Silver
Drs. Meredith & Malcolm Silver
Dr. Carmine Simone
Dr. Carlton G. Smith
Dr. G.E. Douglas Snell
Dr. Kenneth W. Sniderman
Dr. Marja Soots
Dr. Leslie Soper
Dr. John C. Spears
Dr. John C. Stears
Dr. & Mrs. Israel Strashin
Dr. Albert Strickler
Dr. Donald Sutherland
Dr. George Y. Takahashi
Dr. Wayne Tanner
Dr. Ian Tannock
Dr. Lorne M. Tarshis
Dr. Charles Tator
Dr. Ian Taylor
Dr. John R. Taylor
Dr. Ron Taylor
Dr. Hugh Thomson
Dr. Marvin Tile
Dr. George X. Trimble
Dr. Graham Trope
Dr. William Tucker
Dr. Walter P. Unger
Dr. Martin G. Unger
U of T Libraries,
Serials Department
Dr. Murray B. Urowitz
Dr. Shanthi Vasudevan
Dr. James Waddell
Dr. Robert Wald
Dr. Gary D. Webb
Dr. P.M. Webster
Dr. S. Joseph Weinstock
Dr. Richard D. Weisel
Dr. Woodrow Wells
Dr. D. Wesson
Dr. Catharine Whiteside
Dr. E. Douglas Wigle
Dr. Caroline Wright
Dr. James Yao
Dr. Douglas Yates
Dr. Stanley Zlotkin
Dr. Ronald Zuker

ANATOMY AND CELL BIOLOGY

A1

THE NHE-1 REGULATES pH OF PHAGOSOMES IN MACROPHAGES. O.C.Tsai* O.D.Rotstein. Surgical Sepsis Lab, University of Toronto, Toronto ON

Phagocytosis is a process whereby cells engulf extracellular material thereby forming a phagosome. This vesicle fuses with lysosomes, containing hydrolytic enzymes, resulting in degradation of phagosome contents. These enzymes require a low pH for optimal activity hence phagosomal acidification is crucial to eliminate pathogenic organisms.

The sodium-hydrogen exchanger (NHE-1) regulates pH by exchanging a Na+ ion for a H+ ion. We asked whether NHE-1 was 1)present and functional on macrophage plasma membranes and 2)present on phagosomal membranes and functional in phagosomal acidification.

Thioglycollate elicited murine peritoneal macrophages were determined by immunoblotting to contain the NHE-1. Membrane fractionation was performed and the exchanger was found to be an integral membrane protein. Cells loaded with the pH sensitive dye BCECF were shown to recover from an acid load through the activity of the NHE-1 by fluorimetric measurements. By immunonblotting, the NHE-1 was found to be present on isolated phagosomal membrane. In order to detect functional NHE-1 activity, macrophages phagocytosed pH sensitive fluorescein coated *Staphylococcus aureus*. A Na+ concentration gradient was established across phagosomal membrane and phagosomal acidification occurred down to pH 6.0. Phagosomal acidification was also inhibited by the potent NHE-1 inhibitor amiloride.

These data together suggest that NHE-1 is present in macrophages, and translocates to the phagosome during phagocytosis.

BIOCHEMISTRY

B1

DETECTION OF A TAGGED TIK GENE PRODUCT USING RT IN SITU PCR. B. McCormick*, N. Abraham, J.Bell. Ottawa Regional Cancer Centre, University of Ottawa, Ottawa ON, K1H 8L6

This project was undertaken to investigate the feasibility of the novel technique of RT In Situ PCR for the detection of aberrant transcripts for research purposes. The gene product of TIK was chosen for investigation because of the association of some of its mutants with mouse lymphocytic leukemia.

L cells from a human fibroblast line were stably transfected with a tagged wild type TIK gene. Expression of the gene product was confirmed by immunofluorescence. The cells were fixed in formalin, spotted on a glass slide, permeabilized with proteinase K, and the genomic DNA was digested with DNase. The tagged TIK mRNA was subsequently reverse transcribed using a specific 3' primer. The resulting cDNA copies were then subjected to PCR amplification and labelled with digoxigenin conjugated dUTP. After incubation with an antibody and development in a chromogenic solution, all transfected cells exhibited a dark purple cytoplasmic staining. Non-transfected cells were treated similarly and showed only slight staining. A negative control, one in which the RT step was omitted, did not stain. The DNase digestion, RT and PCR steps were all performed on a Perkin Elmer In Situ PCR machine.

The results of this project have proven that RT In Situ PCR is a feasible technique for detecting aberrant transcripts in a research context and has set the stage for development of a screening test for the presence of known pre-leukemic TIK mutants.

B2

STRUCTURAL AND FUNCTIONAL STUDIES OF THE VACUOLAR H^+ - ATPase; THE PROTEIN COMPLEX MEDIATING PHAGOSOMAL ACIDIFICATION

C. Landolt-Marticorena*, P. A. Zawarynski and M.F. Manolson Department of Biochemistry and Division of Cell Biology, Hospital for Sick Children, Toronto, Ontario, Canada.

Vacuolar-type H^+ - ATPases (V-ATPases) have been implicated in the rapid acidification of phagocytic organelles following internalization of microorganisms. The virulence of certain intracellular bacteria has been attributed to their ability to prevent phagosomal acidification, suggesting a critical role for the V-ATPase in combating infection. The V-ATPase complex contains two distinct sectors; a membrane-associated complex (V_0) which functions as the proton channel proper and a peripheral catalytic domain (V_1) responsible for ATP hydrolysis. In *Saccharomyces cerevisiae*, the V_1 sector contains two ATP-binding polypeptides; the 69 kDA subunit involved in ATP hydrolysis and the 60 kDa polypeptide which appears to function as a regulatory domain. ATP•Mg protects the catalytic (69 kDa) subunit from trypsin degradation (range 0.1 to 2.5 µg/mL) in isolated vacuolar membranes. Under comparable treatment conditions (trypsin range 0.05 to 0.25 µg/mL) ATP and ATP•Mg render the regulatory domain (60 kDa) more sensitive to proteolysis. These observations suggest that the catalytic domain and regulatory subunits undergo conformational changes as a consequence of ATP binding and/or hydrolysis. At the moment, experiments are underway to determine if the structural changes observed for the regulatory subunit are due to the direct binding of ATP or as an indirect effect of the catalytic cycling of the 69 kDa protein. Photo-affinity labeling of the catalytic subunit with nucleotide analogues are being employed to determine if stabilizing the protein in an ATP-bound conformation has an effect on the structure of the regulatory domain. Bafilomycin, a potent inhibitor of V-ATPases, renders the 69 kDa subunit more susceptible to trypsin proteolysis in the absence or presence of ATP. This destabilizing effect is minimized, but not abolished in the presence of ATP•Mg. Although bafilomycin bind specifically to the membrane-associated V_0, inhibitor binding results in conformational changes within the peripheral V_1 complex indicating that structural information is readily transmitted between the two sectors. Analysis of the structure and function of the V-ATPase multimeric complex is critical in understanding phagosomal acidification.

B3

THE PTP1C PROTEIN TYROSINE PHOSPHATASE REGULATES THE CATALYTIC ACTIVITY OF THE PROTO-ONCOGENIC SRC PROTEIN TYROSINE KINASE. A-K. Somani*, §D. Branch and K. A. Siminovitch. Dept. of Medicine, Immunology and Molecular and Medical Genetics, University of Toronto and Samuel Lunenfeld Research Institute, Mount Sinai Hospital; §Research Section, Canadian Red Cross Society, Toronto, Ontario Canada.

PTP1C is a SH2 domain-containing cytosolic protein tyrosine phosphatase expressed primarily in haemopoietic cells. Recent data from our group have revealed the association of loss-of-function mutations in the PTP1C gene with expression of the murine motheaten (*me*) syndrome, a phenotype associated with severe lymphocyte dysfunction. Based on preliminary data revealing a role for PTP1C in modulating signalling pathways coupling the T cell antigen receptor to cell proliferation, we examined the potential relevance of PTP1C to regulation of T cell src tyrosine kinase activity. Our data revealed that despite the expression of normal levels of src protein, thymic T cells from *me* mice manifest markedly diminished and essentially negligible levels of src kinase activity relative to the levels detected in wild-type thymic T cells. This finding together with the observation that PTP1C coprecipitates, and thus appears to physically associate with src, suggest that PTP1C induced dephosphorylation of src may be required for expression of src kinase activity. This contention is supported by the observed capacity of recombinant PTP1C to dephosphorylate recombinant src and src immuoprecipitates from normal thymic cells and to restore catalytic activity to src immunoprecipitates derived from *me* thymic cells. Together these data suggest that PTP1C acts to dephosphorylate the kinase inhibitory phosphorylated tyrosine loacted in the src carboxy terminus and as such plays a critical role in regulating the functional capacity of the src tyrosine kinase in T cells.

B4

A MODEL FOR THE STRUCTURE OF TRANSMEMBRANE SEGMENTS: MUTATIONAL ANALYSIS OF AROMATIC RESIDUES IN PHAGE M13 COAT PROTEIN. T. Neogi*, M. Glibowicka, C.M. Deber. Biochemistry Research, The Hospital for Sick Children, Toronto, ON, M5G 1X8.

Prediction of a protein's structure and function from its amino acid sequence represents one of the prime objectives of structural biology, the realization of which would help illuminate a whole spectrum of disease mechanisms from a protein conformational perspective. Despite the role of membrane proteins in many cellular processes, little is known about the molecular details of their structural organization. A coat protein of the filamentous bacteriophage M13 provides a simple model for studying such properties in a membrane-spanning protein domain. Its simplicity lies in the fact that it is only 50 amino acids long and inserts itself into the inner membrane of its host bacterium as a single spanning α-helix. By altering certain critical amino acid residues, we hope to gain insight into the structural and functional implications of those amino acids. Specifically, we are investigating the mutability of two amphipathic aromatic residues — Trp26 and Tyr21. These two residues are thought to confer stability to the native α-helix structure at the membrane-solvent interface. Trp26 is conserved throughout the filamentous phage family and is thought to be nonmutable by previous randomized mutagenesis studies. We sought to determine definitively the mutability of this residue by saturation site-directed mutagenesis. Oligonucleotides, constructed such that all possible amino acids could occur at the Trp26 site, were annealed to wild type M13 DNA. Following transformation of host *E. coli* bacteria with DNAs incorporating the synthesized oligonucleotides, the resultant viral DNAs were sequenced using dideoxynucleotides to detect any mutations that may have occurred. Screening of 100 viral plaques has shown no viable Trp26 mutants, consistent with an absolute requirement for tryptophan at this site. Similar experiments carried out at the Tyr21 site have yielded five novel mutants: Y21L, Y21V, Y21I, Y21T, Y21F. Each substituted amino acid has at least one of tyrosine's characteristics; each is either hydrophobic, aromatic, or has a hydroxyl group, indicating there are some minimum requirements at this site.

B5

EXPONENTIAL AMPLIFICATION SEQUENCING. D. M. Hwang*, R.-X. Wang, and C.-C. Liew. The Cardiac Gene Unit, Department of Clinical Biochemistry, University of Toronto.

In order to sequence lambda phage cDNA clones directly from single plaques, we have developed a method, which we defined as a single stage exponential amplification sequencing (EAS). By coupling PCR with cycle sequencing in one step, EAS uses exponential amplification, rather than linear amplification, to generate sequence data from a very small quantity of DNA template.

We have applied EAS in our laboratory to the sequencing of single plaques from Lambda ZAP-Express cDNA libraries. Plaques were picked and eluted in 100 μL elution buffer, of which 1 μL was used for EAS. Average length of readily sequenced cDNA inserts was approximately 500-1100 bp, as determined by PCR. Our results indicated a decrease in the template requirement of at least 80-fold from standard cycle sequencing protocols. Despite this decreased requirement, sequence reads of between 200 and over 600 bp were obtained. One sequence, for example, was compared to known sequences in Genbank and found to be 99.8% identical over 526 bp with a hydrophobic protein encoded by the mouse mitochondrial genome.

This method to date has been successfully applied only to relatively short cDNA inserts (500-1100 bp). The dNTP/ddNTP ratios may be a critical factor in optimizing EAS conditions to permit sufficient amplification at longer insert lengths.

Because of its potential to cut both costs and labor involved in template preparation and to decrease the quantity of template required for sequencing, EAS would be of potential interest not only to large scale sequencing projects, but also to the field of molecular diagnostics.

B6

PURIFICATION AND CHARACTERIZATION OF TS28, A NOVEL PROTEIN LOCALIZED TO THE TRANSVERSE TUBULES OF SKELETAL MUSCLE. C.A.E.Mason*, M.Rodriguez, D.Mochly-Rosen, A.O. Jorgensen. Department of Anatomy and Cell Biology, University of Toronto, Toronto, Ontario, M5S 1A8 and Department of Molecular Pharmacology, Stanford University, School of Medicine, Stanford, California, U.S.A. 94305-5332.

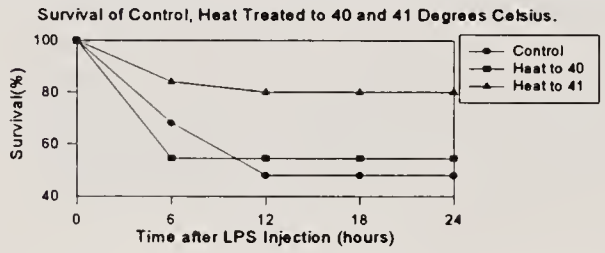
TS28 is a 28 kDa integral membrane protein localized to skeletal muscle transverse tubules (TTs) where it is first detected at the onset of their de novo formation. Although the function of TS28 is not known, its localization to the TTs as they begin to form suggests that it may be essential in TT biogenesis and/or excitation-contraction coupling. Regarding its potential function, it has been suggested that TS28 may correspond to 1) a 28 kDa small GTP binding protein (J. Biol. Chem. 266:17613) and/or 2) a 28 kDa substrate of protein kinase C (Biochem. Biophys. Res. Comm. 196:1073), previously identified in isolated TT membranes. To test these hypotheses we have purified TS28 by immunochromatography and examined its ability 1) to function as a substrate for protein kinase C and 2) to bind [α-^{32}P] GTP in a blot overlay assay. Initial studies show that TS28 is a substrate for exogenous protein kinase C. Studies are in progress to determine whether TS28 is a substrate for a protein kinase C isozyme intrinsic to T-tubules in skeletal muscle. However, purified TS28 does not bind [α-^{32}P] GTP using a blot overlay assay. To characterize the structure of TS28 we have purified microgram quantities of highly purified protein for amino acid sequence analysis of internal peptides. This will permit us to design oligonucleotide probes for the purpose of cloning the cDNA encoding TS28. Availability of the cDNA encoding TS28 will facilitate molecular biological approaches designed to determine the function of this TT protein. (Supported by MRC (A.O.J.) and by NIH (D.M.-R.))

BIOCHEMISTRY

B7

THE EFFECTS OF THE STRESS RESPONSE IN A RAT MODEL OF SEPSIS E.K. Chu*, S.P. Ribeiro, A.S. Slutsky, Respirology Laboratory, Faculty of Medicine, University of Toronto.

It has been shown that heating an animal for a brief period of time to a few degrees above its normal body temperature activates the body's stress response which in turn can protect against lethal stimuli. The stress response is characterized by a transient down-regulation of most cellular products and the up-regulation of heat shock proteins (HSP72). Studies of this stress response have focused on its induction *before* the administration of a lethal stimulus. However, the stress response would be of therapeutic value if it were shown to be protective after the occurrence of sepsis. The objective of the present study was to investigate the protective effects associated with the induction of the stress response *after* the intravenous injection of the bacterial endotoxin lipopolysaccharide (LPS). Sixty-one Sprague Dawley rats were injected intravenously with *Escherichia coli* lipopolysaccharide (15mg/kg). They were then randomly divided into three groups and given the following treatment: 1) no treatment (control group), 2) heated to 40°C, 3) heated to 41°C. Western analysis using antibodies directed against HSP72 demonstrated significant expression of HSP72 in the lungs of rats heated to 41°C. Lesser amounts of HSP72 were detected in the lungs of rats heated to 40°C. Survival rates in the rats heated to 41°C, 20/25 (80%), were higher than those of the untreated rats, 12/25 (48%) ($p=0.039$). These findings demonstrate that producing the stress response after LPS injection is associated with the induction of HSP72, and can protect rats from the lethal activity of LPS.



B8

CLONING AND CHARACTERIZATION OF A HUMAN GENE ENCODING A NOVEL G PROTEIN-COUPLED RECEPTOR Michael Heiber*, Adriano Marchese, Tuan Nguyen, Susan R. George and Brian F. O'Dowd. Department of Pharmacology, University of Toronto

The elucidation of the molecular mechanisms underlying the functioning of the endocrine system is proceeding at a rapid rate. This has been facilitated by the cloning and characterization of the genes encoding a number of different hormones and receptors, permitting the detailed pharmacological and biochemical analysis of these proteins. During this undertaking, it was observed that the structure of many different hormone receptor proteins are very similar. The most salient features include 7 transmembrane domains and numerous conserved amino acids. These receptors have been grouped into one large superfamily called G protein-coupled receptors (GPCR).

We sought to identify novel hormone receptors by cloning and characterizing the respective genes. We proceeded by designing degenerate oligonucleotide primers based on conserved regions in genes encoding previously cloned GPCRs. These primers were used in the polymerase chain reaction (PCR) to amplify human genomic DNA. This resulted in the identification of one unique PCR product, which was subsequently used as a probe to screen a human genomic DNA library. Seven probe-binding phage clones from this library were purified and the inserts were characterized by Southern blot analysis. A 1700 bp fragment from one of the phage clones was subcloned and the insert was sequenced and found to contain the complete coding region of a novel gene we have named GPR15.

Analysis of the translated amino acid sequence of GPR15 revealed 7 hydrophobic regions corresponding to 7 transmembrane domains as well as the highly conserved DRY sequence in the second intracellular loop. In addition, the amino acid sequence of GPR15 shares sequence identity with other GPCRs, most notably the angiotensin II AT1 and AT2 receptors, and the interleukin 8b receptor further indicating that this gene encodes a novel GPCR.

In summary, we have cloned and characterized a human gene encoding a potentially novel hormone receptor. Although the specific nature of the endogenous ligand which binds to GPR15 is currently unknown, future experiments will involve expressing GPR15 and testing different hormones and other ligands for specific binding to this receptor.

CARDIOLOGY

C1

IS MULTIPLE INTRACORONARY STENTING AS SAFE AS SINGLE STENTING? C. Boulé*, G. Devlin, and C. Lazzam. The Toronto Hospital, Toronto, Ontario, Canada.

A total of 227 stents were delivered to 184 lesions during 167 procedures in 163 patients from April 1994 to June 1995 (13% of all PTCA). Multiple stents (MS) were placed in 35 lesions (19%) in 35 cases and single stents (SS) in 149 lesions (81%) in 133 cases. Lesion types in the MS vs. SS group were as follows: A=3% vs. 6%, B1=11% vs. 16%, B2=17% vs. 31%, C=69% vs. 47%. Indications for stenting (MS vs.SS) were, de novo=9% vs. 11%, restenosis=14% vs. 22%, suboptimal result=17% vs. 25%, dissection=40% vs. 26%, acute closure=9% vs. 4%, vein graft=11% vs. 12%. In hospital complications are shown below.

Complications	MS (%), n=35	SS (%), n=133
Acute or Subacute closure	2 (11)	4 (4)
MI (enzymes or EKG)	5 (14)	6 (5)
CABG	1 (3)	4 (3)
Death	0 (0)	2 (2)
Any complication	7 (20)	14 (11)

No significant difference was noted in overall complications (p=ns). Warfarin was considered unnecessary in 49% of MS and 53% of SS cases. A trend toward increased frequency of myocardial infarction in the MS group may reflect the fact that multiple stents were placed in longer, more complex lesions, and most frequently as treatment for dissection.

Conclusions: Multiple stent placement is performed as safely as single stenting and does not require increased anticoagulation.

C2

LONG TERM SURVIVAL IN PATIENTS WITH EISENMENGER'S SYNDROME. J.S. Moussadji*, D.A. Harrison, W.J. Cantor, M.S. Connelly, G.D. Webb, P.Liu, P.R. McLaughlin, S.C. Siu. The Toronto Congenital Cardiac Centre for Adults, The Toronto Hospital, University of Toronto.

Prognostic determinants for adults with Eisenmenger's syndrome have not been established. We reviewed the outcome of 106 adults with Eisenmenger's syndrome (age 29 +/- 11 yrs, 42% male) assessed at the Toronto Congenital Cardiac Centre for Adults. Median follow-up was 6.1 years. Baseline clinical and ECG data were correlated with mortality during the follow-up period.

Results: 66 patients (62%) have simple cardiac anatomy (14 atrial septal defect, 43 ventricular septal defect, 9 patent ductus arteriosus). The remainder have complex cardiac anatomy (including atrioventricular septal defect, truncus arteriosus and transposition of the great arteries).

There were a total of 27 deaths. The Kaplan-Meier survival curve is displayed. Median survival was 53.0 years.

Patient baseline characteristics were analyzed to determine features associated with mortality. Cox regression analysis identified complex anatomy ($p=0.02$) and maximum precordial ECG voltage (sum of largest R in leads V_1 - V_3 and largest S in leads V_4 - V_6) ($p<0.03$) as independent predictors of mortality.

Conclusion: Baseline characteristics can identify increased mortality risk in patients with Eisenmenger's syndrome. These prognostic data may be useful in assessing patients for transplantation.

C3

MYOCARDIAL GLUTATHIONE IN PRECONDITIONING PROTECTION AGAINST ISCHEMIC INJURY. Atul Verma*, Neelam Singh, Pawan K. Singal. Division of Cardiovascular Sciences, St. Boniface General Hospital Research Centre, University of Manitoba, Winnipeg, MB, R2H 2A6.

Levels of myocardial glutathione as well as its probable role in preconditioning protection against ischemic-reperfusion (I-R) injury were studied in isolated, perfused rat hearts. Isolated hearts were subjected to 60 min of global I and 40 min R. For preconditioning, hearts were exposed to 5 min global I and 25 min of R before subjecting them to longer I-R durations. As expected, preconditioning offered a significant protection against I-R induced contractile failure as well as rise in resting tension. Control as well as preconditioned hearts were analyzed for reduced glutathione (GSH) levels before I, after I, and after I-R. I-R without preconditioning caused a significant reduction in GSH levels and this effect was modulated in preconditioned hearts. Thus, a positive correlation between force recovery and retention of GSH after 60 min I and 40 min R was seen. In order to examine whether GSH preservation was a cause or an effect of the preconditioning protection, myocandal GSH levels were depleted by treating rats with L-buthionine-S,R-sulfoximine. In these GSH depleted hearts, preconditioning protection against I-R was significantly less. The study suggests a protective role of GSH in preconditioning protection.

CO1

RURAL ATTITUDES TOWARD AND METHODS OF MALARIA PREVENTION IN CHILDREN IN SAVALOU, REPUBLIC OF BÉNIN. C.Q.T.Lee*, S.Rashed, C.C.Gbaguidi, S.Lalaye, S. Capochichi. Projet Moustiquaire Impregnée Préventive, B.P.95, Savalou, Benin and International Health Programme, University of Toronto, Faculty of Medicine

Malaria transmission follows a hyperendemic pattern in the rural Savalou region. Understanding socio-cultural factors and attitudes may be valuable in rendering malaria prevention schemes more effective for children.

190 individuals from 8 randomly-selected villages participated in separate-sex focus group discussions. In-depth interviews with 16 key informants followed after content analysis of the focus group discussions. They were asked to discuss about their attitudes toward malaria causation, prevention, and treatment, particularly as they relate to children.

Respondents commonly considered their children to be most vulnerable to malaria. Malaria was perceived to be caused by multiple agents: 1)sun 2)mosquito 3)excessive heat from the fire 4)overconsumption of peanuts. Many respondents do not connect malaria with the mosquito in theory or practice. Although malaria prevention is not widely practiced, methods most frequently utilized were 1)daily infusions of various leaves and roots 2)mosquito nets 3)chloroquine. Many participants, especially women support monthly payment or credit schemes to encourage the purchase of insecticide-impregnated mosquito nets. Culturally sensitive and innovative approaches to malaria education and to universal accessibility of mosquito nets are important for prevention of malaria in children.

CO2

THE RELATION OF CONJUNCTIVAL PALLOR TO THE PRESENCE OF ANEMIA. T. N. Sheth*, N. K. Choudhry, A. S. Detsky Department of Medicine and Clinical Epidemiology, The Toronto Hospital, University of Toronto.

Conjunctival pallor is commonly used as a clinical sign of anemia. The value of this test depends on the relationship between conjunctival pallor and the actual hemoglobin status of the patient. In this study, our objectives were to determine the validity and reliability of this clinical assessment.

Methods: A prospective study of 208 general and subspeciality medical patients in The Toronto Hospital was undertaken. Patients with hemoglobin measured within three days of observation without intercurrent tranfusion were included. Three independent and blinded observers assessed conjunctival pallor as being present, borderline, or absent. Anemia was defined as a hemoglobin concentration of less than 90 g/L. Likelihood ratios were calculated as a measure of validity and reliability was measured by kappa scores of agreement between paired observers.

Results: Likelihood ratios, calculated on the basis of observations by Observer 1, were: pallor present = 3.43, pallor borderline = 1.11, pallor absent = 0.53. Mean kappa score between paired observers was 0.56 (range=0.55-0.58)

Conclusions: The presence or absence of conjunctival pallor does not significantly alter the probability that a patient has or does not have severe anemia (Hg <90g/L) respectively. That is, patients with severe anemia commonly do not display conjunctival pallor and patients without anemia may have pale conjunctiva. The reliability of this clinical sign is moderate. This study suggests that conjunctival pallor has a limited role in the clinical assessment of anemia.

COMMUNITY MEDICINE AND EPIDIMEOLOGY

CO3

EVALUATION OF A PLASMA SEPARATOR CARD USED IN CONJUNCTION WITH THE RAPID PLASMA REAGIN TEST FOR THE DIAGNOSIS OF SYPHILIS. Sandy L. Dong*, J. O. Ndinya-Achola, and Stephen Moses, University of Toronto, Toronto, Ontario, Canada and University of Nairobi, Nairobi, Africa.

Objective: To evaluate the effectiveness of a newly developed plasma separator card as a means of obtaining adequate blood plasma for serological testing for syphilis using the rapid plasma reagin (RPR) test.

Methods: Blood samples were obtained from STD patients attending the Nairobi City Council Special Treatment Clinic. Both a finger-prick sample and a venous blood sample were taken from each patient. Serum from the finger-prick sample was obtained and tested using the separator card the RPR test on site. Venous blood was centrifuged and the serum tested for syphilis using the RPR test once on site and again at the laboratory at the Department of Medical Microbiology, University of Nairobi. Any patient who tested positive by RPR in the clinic or laboratory has a confirmatory Treponema Pallidum Hemaglutination Antibody (TPHA) confirmatory test performed. The patients were treated according to the test results obtained on site.

Results: A total of 137 patients were recruited, 67.2% were males and 32.8% were females. Adequate amount of serum was collected from the plasma separator card 97.8% of the time. The sensitivity of the RPR test using the separator card was found to be 85.3%, the specificity was 95.0%, and the positive predictive value was 85.3% when compared to the RPR test using serum obtained by centrifuged venous blood at the clinic.

Conclusion: The plasma separator card represents a safer and simpler method of obtaining serum for syphilis testing then centrifugation of venous blood, obviating the need for needles and syringes, a centrifuge, and electricity. The results of this study are promising. However, further evaluations of the card are required in a variety of settings, including rural areas, before it can be recommended for widespread use.

DIET AND NUTRITION

D1

RATIO OF ANIMAL/VEGETABLE PROTEIN PREDICTS CHANGE IN RISK FACTORS FOR CORONARY HEART DISEASE. TPP Ransom*, T Nikain, L Augustin, DJA Jenkins. Dept Nutr Sci, Univ of Toronto.

Background Dietary recommendations for lowering blood cholesterol levels and decreasing the risk for coronary heart disease (CHD) include reducing the intake of saturated fat and cholesterol and increasing the intake of polyunsaturated fat and fibre. Such maneuvers would affect protein source in the diet which may act independently at altering CHD risk factors.

Hypothesis Decreases in the animal/vegetable (A/V) protein ratio relate favourably to changes in blood lipids and clotting factors.

Methods An existing nutrient data base was modified to include values for animal and vegetable protein. Results are from twelve hyperlipidemic volunteers originally in a study designed to study physiological effects of dietary fibre. Changes, from baseline to being on a high fibre diet, in blood lipids and clotting factors were compared to changes in the A/V ratio.

Results The A/V ratio on the high fibre diet (0.3) was lower (1.2±0.2, $p<0.001$) than on the baseline diet. Significant reductions were also observed for saturated fat and dietary cholesterol. Total cholesterol, low density lipoprotein cholesterol (LDL-C), HDL-C, apolipoprotein A1 (apo A1) and apo B were reduced: 0.5±02 mmol/L, $p<0.02$; 0.4±0.2 mmol/L, $p<0.10$; 0.1±0.0 mmol/L, $p<0.02$; 0.1±0.0 g/L, $p<0.02$; and 0.1±0.0 g/L, $p<0.10$ respectively. Factor VII was reduced (26.3±4.7 %, $p<0.001$) and tissue plasminogen activator (tPA) was increased (3.8±1.5 mu/mL, $p<0.05$). Changes in the A/V ratio related to changes in apo B ($r=0.673$, $p=0.017$) and changes in tPA ($r=-0.765$, $p=0.004$). No other significant correlations were observed.

Conclusions The A/V ratio is an independent predictor for apo B and tPA. Future dietary recommendations for lowering CHD risk might include decreasing protein from animal sources while increasing protein from vegetable sources.

D2

THE EFFECTS OF HIGH SOLUBLE FIBER DIETS ON BREATH HYDROGEN AND METHANE, SYMPTOMATOLOGY AND FECAL OUTPUT. TL Znajda*, DJA Jenkins, AV Rao, SJ Mitchell, TMS Wolever, RA Hegele, C Mehling, L Katzman Relle, TPP Ransom, DL Boctor and P Wursch. Department of Nutritional Sciences, U of T.

To determine the effects of high fibre diets on colonic function we studied the relationship of day-long (12 h) breath hydrogen (H_2) and methane (CH_4) levels to changes in fecal weight and symptoms of carbohydrate malabsorption. Forty three mildly hyperlipidemic volunteers (15 men, 28 post-menopausal women) randomly consumed two 4-month metabolic diets, one high in soluble fibre foods, known to have blood lipid lowering effects, and the other high in insoluble fibre, considered to be lipid neutral. Diets were high in fibre (>2.5 g/100 kcal) and low in fat (<20 %).

On the soluble fibre diet, the mean day-long H_2 levels at weeks 2, 4, 8, 12, and 16 were 12±5 % lower than on insoluble fibre ($p<0.02$), while methane levels tended to be higher (119±32 %, $p<0.001$). With the soluble fibre foods, day-long H_2 levels remained constant over the 16 weeks. Maximal changes in breath gases were attained by 4 weeks and thereafter remained constant. No difference was seen in wet fecal weights between diets, but symptoms of flatulence and abdominal distension were higher on the soluble fibre diet at week 15 ($p<0.001$ and $p<0.01$, respectively).

We conclude that high levels of high fibre foods with lipid lowering potential were well tolerated. Furthermore, symptoms of increased colonic fermentation were not reflected in increased H_2 levels over the day, possibly because of changes in microflora metabolism and increased short chain fatty acid generation.

D3

DIETARY FACTORS AND BREAST CANCER IN JAPAN AND CANADA

BJ Willcox*[1], DJA Jenkins[1], K Fuchigami[1], DC Willcox[1], TP Ransom[1], N Tariq[1], CWC Kendall[1], M Suzuki[2], H Todoriki[3], S Kinjo, H Komatsu[4], S Nakahara[5], R Mibu[5]. Dept of Nutr Sci[1], Univ of Toronto; Depts of Comm Health[2] and Prev Med[3], Univ of the Ryukyus; Dept of Anesthes and Emerg Med[4], Kagawa Medical School; First Dept of Surg[5], Kyushu University, Japan.

Japan has among the world's lowest incidence of and mortality rates from breast cancer. In Canada, however, breast cancer is one of the leading causes of death in women. Migration studies have shown that environmental mechanisms, such as dietary factors, are extremely important. Although the etiology is not known, hormonal factors, especially estrogens have been strongly linked to this disease. Recent evidence suggests that hormonal activity may be altered by several dietary macro- or micro-nutrients including fat, fiber, and polyphenolic dietary anti-estrogens (eg isoflavone phytoestrogens). There is tremendous variability in the levels of these dietary factors between Japan and Canada. Thus, we studied the potential connection between specific dietary factors, especially dietary anti-estrogens, and breast cancer in Japan and Canada. Sixty healthy Japanese women between the ages of 30-95 were selected from urban and rural areas of Japan. Dietary records were made of their regular diet. Measurements included height, body weight, blood pressure, fasting serum, and 24h urine. These volunteers were compared to Canadians taking part in mutual studies in Toronto. Japanese volunteers consumed significantly lower levels of dietary fat, higher levels of carbohydrate and soy products than their Canadian counterparts ($p<0.01$). The Japanese also had significantly greater intake of dietary anti-estrogens ($p< 0.01$). The large intake of dietary anti-estrogens of the isoflavone class, mainly from soy products, suggests a potential dietary mechanism for the low incidence of breast cancer in the Japanese.

E1

THE EFFECTIVENESS OF THE UNIVERSITY OF TORONTO IN-TRAINING EVALUATION REPORT TO MEASURE THE CLINICAL COMPETENCE OF SURGICAL RESIDENTS.

G. Zahariadis* University of Toronto, Toronto, ON

There are several unique aspects of clinical competence (CC) which cannot be appropriately measured by written examinations. Some of these "difficult to measure" attributes of CC include communication skills, rapport with patients, responsibility e.t.c. Thus, accurate and fair assessment of CC is important for all faculty assessing it.

The University of Toronto-Department of Surgery in training evaluation report (ITER) was an instrument developed to evaluate surgical residents (SR) CC. The purpose of this study is to assess this instrument.

1527 ITER grades and principles of surgery (POS) exam results of 236 SR (mean=6 ITER/SR) since 1989 were analyzed (1) to compare and contrast SR grades in different specialties; (2) to analyze individual EV grading practices; (3) to determine if SR grades improve as they progress; (4) to determine if there is any correlation between ITER grades and POS scores; (5) to identify deficiencies in this grading practice and (6) to determine the factor structure.

Preliminary results indicate that SR marks cluster and that most EV are reluctant to use the low end of the scale. One-way-ANOVA results indicate there are significant differences between grades in different surgical subspecialties. There is poor correlation between ITER grades and POS scores. Furthermore, ITER grades do not reflect improvement as SR advance. The converse frequently occurs. Two factors emerged across all subspecialties and the group as a whole.

There is little order and regularity in grading practices indicative of very poor interrater reliability. There is a high internal consistency of grades which likely represents that a resident gets evaluated equally on all CC criteria when instructors are usually aware of only a couple. This ITER is flexible, cheap, unobtrusive, provides the potential for feedback and has the ability to evaluate "difficult to measure" CC attributes. It has excellent face validity; however it suffers serious deficiencies in terms of evidence for construct validity and reliability. This is likely a reflection of EV lack of understanding on how to properly complete the ITER. Residency programs should provide adequate evaluating instructions for faculty to ensure that this ITER is of value.

E2

• PUBLIC HEALTH AND THE EDUCATION OF TUBERCULOSIS PATIENTS IN TRANSKEI.

•Canadian Society for International Health*, W. Harris and C. Cheng. All Saints Hospital, Engcobo, Eastern Cape Province, Republic of South Africa.

• An estimated 60 000 South Africans develop tuberculosis annually and many times that number are infected by *M. Tuberculosis*. Disadvantaged blacks are disproportionately affected, yet despite the election of a multi-racial government, public health programs combating TB in black communities still languish short of resources. This study evaluated efforts to educate tuberculosis patients about TB. The study was conducted at a peripheral referral hospital in rural Transkei (a mainly black region with a high prevalence of tuberculosis). Forty-five patients and ten health workers were interviewed using standardized questionnaires. Questions probed existing programs, assessed patient perception of TB and identified barriers to compliance. Patients were randomly selected and interviewed using interpreters. 91% of patients knew they had TB, yet few could comment on the disease or treatment. Although health workers generally felt that all patients received education only 8.9% of patients recalled being told how long treatment lasts, and a mere 24.4% remembered being educated about the cause of TB. Only 47.7% of patients claimed to understand the reasons behind the advice health care workers gave. Analysis revealed that patients who recalled education knew more about TB than their peers.

Health educators traditionally divided their time between community-based and in-patient programs. However, shortages of transportation and personnel have hindered efforts in the community. However, fiscal restraints make more resources unlikely. The researchers therefore recommend concentrating efforts in the hospital where patients are diagnosed and quarantined. This approach may alleviate the need for transportation and efficiently utilize personnel. Focusing upon in-patient programs is not ideal, but more economical use of resources may achieve better results. However, the feasibility of this suggestion must be researched. Tuberculosis is a disease of poverty. Until socioeconomic barriers affecting the health of disadvantaged groups disintegrate, TB will remain a serious problem. Nevertheless, effective education is an integral first step towards empowering the disadvantaged.

E3

WOMEN AND CARDIOVASCULAR DISEASE-KNOWLEDGE BASE OF THE FEMALE ADOLESCENT POPULATION IN METRO TORONTO Reena Lovinsky*, Dr. D. Stewart, Women's Health Program, The Toronto Hospital, Toronto, Ontario

Cardiovascular disease (CVD) is a significant issue for women's health since it is the leading cause of female mortality in Canada, has a large impact on Canada's economy and because special risk factors exist for women that increase their risk of developing myocardial infarction and strokes. Since many of the risk factors for heart disease are modifiable and develop in adolescence, it is important that young women are aware of their risk of developing CVD and that it can be changed. A questionnaire evaluating knowledge of CVD and its prevention was distributed to 181 female students at two high schools in Metropolitan Toronto. Answers revealed gaps in knowledge about the prevelence of CVD among women and its modifiable risk factors. More education is needed to fill the gaps in heart health knowledge that exist in Toronto's youth and high schools should be encouraged as "mini-communities" to promote heart health.

E4

ATTITUDES OF PHYSICIANS TOWARDS THE ONTARIO BREAST SCREENING PROGRAMME

G. B. Vohra*, P. Chart. Sunnybrook Health Science Centre. North York, Ontario, Canada.

The Ontario Breast Screening Program (OBSP) provides early detection services to decrease mortality and morbidity from the leading cancer among women. Their services include breast self examination education, a clinical breast examination and a mammogram. Abnormal screening results are sent first to the physician with recommendations for assessment that may include: radiological, & pathological tests, and a surgical consultation. The purpose of the study was to: 1. Examine current referral practices of community physicians in order to identify barriers to referral 2. Examine attitudes towards the OBSP to evaluate the program and 3. Identify issues regarding a proposal to add an assessment clinic at the North York Screening Centre in response to improperly managed cases. This study was designed to be a preliminary step to identify significant issues to be addressed in a subsequent large scale survey. The study was conducted by interviewing 7 community physicians for 20-40 minutes in person, or by telephone in a semi-structured format.

Seven interviews were completed. Results indicate that the referral rate is quite low, due to both physician and patient barriers. Most physicians feel the OBSP is providing quality service to their patients. With respect to the proposal for a diagnostic clinic, although there are concerns about lack of contact with patients, and the quality of the staff in the diagnostic clinic, most physicians viewed the proposal positively.

E5

PREVENTION OF NEURAL TUBE DEFECTS WITH FOLIC ACID: DO PHYSICIANS DELIVER THE INFORMATION TO THEIR CLIENTS? V.S.Perelman‡N.Singal‡G.Koren.Motherisk.HSC,UofT., Toronto, M5G IX8.

Neural Tube Defects (NTDs) are among the most debilitating congenital malformations. Periconceptional folic acid supplementation (PFAS) may prevent 50% to 90% of NTDs. Previous studies demonstrated that the majority of women were not aware of PFAS. However, the awareness and actual pattern of delivery of this information by the primary care physicians has never been analyzed.

We investigated the current level of awareness regarding PFAS by interviewing 36 family physicians who contacted Motherisk by telephone and by analyzing responses of a randomly selected group of 35 primary care practitioners to a distributed questionnaire. Results show that as high as 40% of primary care doctors do not mention PFAS during the discussion of women of childbearing age, or those who are planning a pregnancy. Furthermore, only 14% of the assessed physicians had a complete knowledge of appropriate timing and dosage of folate supplementation.

Our findings indicate that efforts for increasing awareness of PFAS among medical and subsequently non-medical communities should be continued with increased vigour.

E6

A CME PROGRAM EVALUATION OF THE "PSYCHOTHERAPY IN PRIMARY MEDICAL CARE EDUCATIONAL SERIES". V. Sarabia*, Pare, M. F., and Van Lierop, M.. The Department of Family Medicine Sunnybrook Health Science Centre, the University of Toronto Medical School and The Medical Clinic *for* Person-Centered Psychotherapy, Toronto, Ontario, Canada.

Recent studies (Brown and Weston, 1992; Swanson, 1994) have demonstrated that continuing medical education in psychotherapy is both required and desired by many primary care physicians. In an attempt to help fill this need, we developed the "Psychotherapy in Primary Medical Care Education Series" (PPMC). The format and topics covered in these educational sessions were chosen based on a CME needs-assessment in the form of a questionnaire which asked what topics in psychotherapy, psychology and psychiatry were of particular interest to Primary Care physicians (Pare et al., 1994). Also the preferred meeting time, future topics of interest, and general suggestions were determined. The resulting CME series has been underway for the past year and feedback has been gathered in survey form with the goals of assessing the success of the program, and of further refining the educational series to meet the needs of the participants. A large majority of the participants (80%) gave the program an overall rating of "Above Average" to "Excellent". The topics were deemed to be "relevant to the participant's practice" (84%) and for the majority of sessions, "met stated objectives" (54%) and "satisfied expectations" (60%). In addition, 37% of respondents felt that the sessions "would alter their practice performance". A high degree of satisfaction was expressed with the time allowed for audience participation as well as with the facilities and course organization. Many useful suggestions for future topics of interest were offered including: Anger, Personality disorders, Self esteem issues and cognitive psychotherapy techniques. Currently preparations are underway for the next PPMC educational series. Suggestions and feedback are being actively sought from general practitioners, and other mental health professionals.

References

Brown, J. B. and Weston, W. W. Can. Family Physician, Vol. 38, 1992.
Swanson, J. G. Can. Family Physician, Vol. 40, 1994.
Pare, M. F., *et al.* The General Practice Psychotherapy Association Annual Conference, 1994.

HAEMATOLOGY

H1

PREVALENCE OF HLA CLASS II DR ALLELES IN RESPONDING AND NON-RESPONDING CAUCASIAN PATIENTS WITH CHRONIC HEPATITIS C VIRUS (HCV) TREATED WITH INTERFERON ALPHA-2B. J. P. Wojcik*, J. Wade, M. Margulies, E. J. Heathcote. Regional Histocompatibility Laboratory and Department of Medicine at the Toronto Hospital and University of Toronto, Toronto, Ont. M5T 2S8.

Background: It has been suggested that different class II Human Leukocyte Antigen (HLA) alleles are associated with a susceptibility to develop chronic HCV infection. Hypothesis: Different class II alleles may be associated with different reponses to interferon therapy. Aim: Determine the prevalence of HLA-DR alleles in chronic HCV patients who were responders vs non-responders to interferon therapy.

Methods: 72 Caucasian patients with chronic HCV [M:F 46:26; age 29-67; HCV RNA + by RT-PCR 72/72] seen as outpatients in the Toronto Hospital (Western Division) Liver Clinic were treated with interferon alpha-2b for 3-6 months. "Responders" were those whose previously elevated ALT levels decreased to normal (<40 i.u./l) measured at treatment end. Only Caucasians were studied to avoid ethnic HLA variability. Genomic DNA was isolated from peripheral blood mononuclear cells and amplified by PCR. Reverse line blotting was performed and low resolution class II HLA types were identified by using sequence-specific probes. Alleles (high resolution) were identified using PCR-sequence-specific primers.

Results: The allele prevalences in the 12 alleles observed and tested (DRB1-01,-02,-03,-04,-06,-07,-08,-09,-10,-11,-13,-14) were not significantly different in responders vs. non-responders ($p>0.05$). Conclusions: The prevalences of the low resolution HLA-DRB alleles in responders and non-responders are not significantly different.

H2

ISOLATION AND CHARACTERIZATION OF A SUPPRESSOR-INDUCER FACTOR FROM AN ISOLATED PERFUSED RAT LIVER. Mark J Walsh and John C Marshall. Surgical Sepsis Laboratory, Department of Surgery, Toronto Hospital - General Division and the University of Toronto Medical School, Toronto, Ontario, Canada.

The Isolated Perfused Rat Liver (**IPRL**) has been developed as a model in which to study in vivo, extracorporeal hepatocellular metabolism. Previous studies in this laboratory have identified a factor present in rat plasma after injection of heat killed Pseudomonas aeuruginosa (**PSA**) via the portal vein that induces rat macrophages to produce a second factor. This second factor suppresses lymphocyte proliferation in vitro. The following study was undertaken to establish the **IPRL** as a model in which to produce, isolate and characterize this **SUPPRESSOR-INDUCER** factor.

Anaesthetized, male, 250 gm, Sprague-Dawley rats were infused via the portal vein with 1 mL normal saline (**CON**) or 1 mL of 4 X 10^8 CFU/mL of PSA (**PSA**). After 30 minutes, a total hepatectomy was performed with cannulation of the portal vein and the suprahepatic inferior vena cava. The livers were then perfused with a Krebs-Glucose-HEPES buffer at a rate of 2 - 3 ml/min/g of liver for a period of 3 hours. Aliquots of perfusate were taken at 0, 30 and 180 minutes for blood gas analysis and liver enzyme analysis. The liver enzyme results and blood gas results at 180 minutes are expressed as the mean ± SEM of 6 **CON** and 6 **PSA** animals. There were no statistically significant differences between the two groups by a paired t-test, showing that **PSA** does not impair normal liver function as compared to **CON**.

	AST Units	ALT Units	LDH Units	pH	HCO3 mM
CON	930±302	1086±453	3698±924	7.37±0.01	17.6±0.4
PSA	885±283	776±307	3127±1683	7.35±0.05	16.8±1.7

After the 3 hour perfusion period, the perfusate was collected and concentrated. The concentrate was then characterized on SDS-PAGE, then partially purified on G-75 Sephadex and analyzed for Transforming Growth Factor Beta (**TGF-B**). **TGF-B** is a cytokine that is known to suppress lymphocyte proliferation as well as induce its own release. In a preliminary study, a level of **TGF-B** of 5.16 pg/mL in the **CON** perfusate vs 190.87 pg/mL in the **PSA** perfusate was found. In conclusion, these preliminary studies support the use of the **IPRL** as an appropriate model in which to produce, isolate and characterize this **SUPPRESSOR-INDUCER** factor.

NEUROLOGY AND NEUROSCIENCE

N1

SOUND LOCALIZATION: EFFECT OF VARIOUS STIMULUS PARAMETERS ON ACCURACY AND RESPONSE TIME MEASURES. P. J. Banerjee* and S.M. Abel. Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Ontario

A study was conducted of sound localization ability in normal hearing listeners. The experiment was the first stage in a research program which will investigate the effects of normal aging and pathology of the peripheral and central auditory pathways. Each of the twelve subjects was tested individually in a semi-reverberant sound proof booth that models a real world environment. Sound localization ability was assessed by means of sets of 3, 5, or 7 loudspeakers separated by either 15 degrees or 30 degrees arrayed horizontally in the frontal plane. For each of the six arrays, two separate blocks of listening trials, comprising 20 random presentations of a 300-ms one-third octave noise band, centred at either 500 Hz or 4000 Hz, were presented. Subjects were required to judge the direction of the sound using a handheld response box with a set of microswitches in the same configuration as the loudspeaker array. The correctness of the judgement and the time to respond were recorded for each trial. Statistical analysis of the data indicated that accuracy decreased significantly as both the number of speakers and the separation between speakers increased. Response time increased with number of speakers but there was no effect of speaker span. With increasing laterality of the sound source, accuracy fell but response time was largely unaffected. These findings lend support to the concept of a two stage model of auditory information perception, comprised of sensory analysis and decision making, an aspect of higher order cognitive function.

N2

NEW MODEL ALLOWING BETTER APPROXIMATIONS OF THE BRAIN'S MECHANICAL RESPONSES. O.Mostachfi*, J.Drake, P.Tenti. Neurosurgey. Hospital for Sick Children.

The failure of computer simulations to accurately predict the mechanical response of the brain to such processes as hydrocephalus, head injury, and tumors, stems from a lack of a suitable model, and lack of information about brain mechanical properties. We have developed a simple but realistic brain model which allows us to estimate theses properties.

We assumed that the brain is a porous solid filled by a fluid, a two-phase system. We solved directly the equations for consolidation theory, using simplified brain geometry. Profiles for brain tissue pressure, brain tissue displacement, and brain fluid flow, were generated for chronic compression such as with hydrocephalus. The effects of mechanical properties Young's modulus, shear modulus, Poisson ratio were analyzed.

Solution of this model demonstrates that the response of the brain to mechanical forces is critically dependent on the Poisson ratio, which we estimate to be between .3 and .35 (not .5 as has generally been assumed by others). Brain mechanical response is less sensitive to Young's modulus and shear modulus. We estimate that the shear modulus of normal brain is 5000 N/m^2 by recalculating previous measurements by Metz et al. (1979).

This model explains the failure and instability of previous simulations which assumed that the brain is incompressible (Poisson ratio = .5). Further accurate measurements of the shear modulus are required. Robust and accurate computer simulations will then be possible.

N3

OLFACTORY CONDITIONING IN *C. ELEGANS*. I.Y.M. Wen*, H. Negandhi, S. Runciman, G. Morrison, and D. van der Kooy. Neurobiology Research Group, University of Toronto, Toronto, Canada, M5S 1A8.

The nematode *C. elegans* as is an ideal system to study the cellular and molecular basis for learning and memory because of its simple genetics and well defined neuroanatomy. We have devised a new associative learning paradigm which uses the ability of *C. elegans* to track odors. An attractive odor (diacetyl) is used as the conditioned stimulus (CS) while acetic acid (which is aversive) is used as the unconditioned stimulus (US). Non-food deprived worms are washed onto a fine wire filter and exposed to diacetyl followed by a brief exposure to acetic acid. After six rounds of conditioning, individual worms are tested for their tracking response to a small drop of the CS. A high proportion of naive worms show a tracking response to the CS. However, after conditioning a significant percentage of worms no longer track the CS suggesting that they no longer find it attractive. Several controls have been performed to demonstrate that the failure of conditioned worms to track diacetyl is due to associative conditioning rather than some non-associative process. CS only and US only controls have no significant effect on the tracking response of worms to the CS when compared to the tracking response of naive worms. In addition, explicitly unpaired and pseudo-random pairings have no significant effects on their tracking response. Interestingly, the *lrn-1* and *lrn-2* mutants which were previously isolated using a Na+/Cl- + *E. coli* learning paradigm and have subsequently failed to learn other associative paradigms are also impaired in this task. This suggests that both *lrn-1* and *lrn-2* mutations are necessary for *C. elegans* to acquire several different associative learning paradigms that cross many CS/US boundaries. Finally, the efficiency of this assay will facilitate the screening of large numbers of mutant worms in order to identify novel genes involved in associative learning.

N4

ROLE OF CALPAIN IN THE PATHOPHYSIOLOGY OF SECONDARY INJURY FOLLOWING TRAUMA TO THE SPINAL CORD. PA Schumacher*, JH Eubanks, and MG Fehlings . Playfair Neuroscience Unit, University of Toronto, 399 Bathurst St. mc 12-411, Toronto, Canada M5T 2S8

During the first few hours to days following traumatic or hypoxic injury to central nervous system tissue, secondary biochemical and pathophysiological events cause further destruction of neurons, and represent an important potential site for therapeutic intervention. A rise in intraneuronal [Ca^{2+}] is known to contribute to secondary injury following spinal cord trauma. Using an established rat model for compressive spinal cord injury, we are examining the activation of the Ca^{2+}-activated protease calpain, and the proteolytic degradation of cytoskeletal proteins, in rat spinal cord postinjury. Following laminectomy at T7, a 35 gram compressive injury was applied to the rat spinal cord for one minute, and animals were then sacrificed at the following times postinjury: 15 min, 1 hour, 2 , 4 ,8, 16, and 24 hours. Sham-operated animals, which underwent laminectomy but no injury, served as controls. Using western blot analysis, we have demonstrated a progressive degradation of the cytoskeletal calpain substrate NF200 in whole spinal cord homogenates, with the accumulation of immunopositive NF200 proteolytic fragments within 4 hours postinjury. Immunofluorescent staining with anti-NF200 Ab of paraformaldehyde-fixed sections of injured spinal cord revealed a progressive loss of NF200-positive axons in the dorsal columns and ventral funiculi. We have obtained an antibody specific for spectrin fragments generated by calpain-mediated proteolysis (the kind gift of Cephalon, Inc). This Ab does not recognize native spectrin, nor spectrin fragments generated by other proteases, and istherefore an indirect though specific assay for calpain activity. Western blotting has revealed low calpain activity in uninjured tissue, which progressively increases to a peak activity at 1 - 2 hours postinjury. An investigation of the degradation of other cytoskeletalcalpain substrates postinjury is currently underway. Finally, using a pCRII plasmid vector system, we have cloned a 638 bp fragment of calpain II DNA - a ubiquitously expressed isoform of calpain - from first-strand hippocampal cDNA. *In situ* hybridization studies of rat spinal cord have confirmed the expression of calpain II mRNA in grey matter. Potential changes in the level of calpain II expression postinjury are currently being investigated.

N5

ANALYSIS OF TREMOR-RELATED ACTIVITY IN HUMAN THALAMUS. S.B. Giancola[1]*, J. Tsoukatos [1], W.D. Hutchison [1], R.R. Tasker [2], A.M. Lozano [2], J.O. Dostrovsky [1] . Depts. of [1]Physiol., and [2]Surgery. Univ. of Toronto, M5S 1A8, Toronto, Canada.

Parkinson's Disease (PD) is a common neurological disorder characterized by rigidity, akinesia, bradykinesia, postural reflex impairment and tremor. Most symptoms of PD are due primarily to loss of dopaminergic neurons in the substantia nigra, however the mechanisms mediating tremor are unclear but likely involve the thalamus. Recently, three types of neurons responding to afferent inputs, to voluntary movement and non-responding have been shown to fire in synchrony with tremor. The purpose of this study was to analyze firing patterns of tremor cells (TCs) found in the thalamus of PD patients, and in particular to determine whether those not responding to afferent inputs, might be generating the tremor by an intrinsic oscillation involving an underlying calcium spike. Analysis of burst structure, calculation of autocorrelograms, interval time histograms, interburst time and intraburst time histograms was performed on 48 TCs obtained from seven patients undergoing stereotactic surgery. Intraburst firing patterns in all three types of TCs indicated that a calcium spike was not involved, suggesting that intrinsinc oscillatory membrane properties were not contributing to the tremor related activity. In addition, the three subtypes of TCs were found to be localized in different areas of the thalamus. These findings further our understanding of the role of thalamus in mediating tremor. (Supported by the Parkinson's Foundation of Canada)

N6

CYTOKINE MODULATION OF NERVE GROWTH FACTOR EXPRESSION BY ASTROCYTES. A. Armour*, T. Boutros and V.W. Yong. Neuroimmunology Unit, Montreal Neurological Institute, McGill University, Montreal, Qc.

In seeking to explain the therapeutic efficacy of IFN-β (Betaseron^{R}) in MS, it has recently been shown that IFN-β increases the production of NGF by astrocytes. Of interest with respect to the treament of multiple sclerosis, NGF has been shown to modulate B and T lymphocyte function as well as stimulate oligodendrocyte proliferation and process extension, both critical to the formation of myelin. This finding may also have significant clinical implications in Alzheimer's disease, where the extensive degradation of NGF-dependent cholinergic neurons is pathogenic. Reactive gliosis, where astrocytes undergo proliferation and hypertrophy, is a prominent feature following many types of injury to the CNS, and is mediated by specific inflammatory cytokines (IFN-γ, IL-1β, IL-2, IL-6, TNF-α, TGF-β_1). Reactive astrocytes secrete a range of neurotrophic molecules, including NGF, around the locus of a lesion. In order to better assess the role of inflammation in the CNS, this study examines the effect of different inflammatory cytokines, besides IFN-β, on the secretion of NGF by astrocytes in culture.

In order to achieve this, neonatal mouse astrocytes and human fetal astrocytes were exposed *in vitro* to different concentrations of IL-1β, IL-2, IL-5, IL-6, IFN-β, IFN-γ, TNF-α and TGF-β_1 for six hours each. Northern blots of total RNA were hybridized with either species-specific or cross-reactive, radioactively end-labelled cDNA probes to NGF mRNA. Levels were then quantified by phosphoimaging.

We found that, in contrast to IFN-β's two-fold stimulation of NGF mRNA expression at 300 U/ml, IL-1β at 100 U/ml increased murine astrocyte NGF expression 1.5-fold, and IFN-γ at 100 U/ml produced a 2.5-fold increase over control. IL-2, IL-5, TNF-α and TGF-β_1 did not produce any significant effect in mouse astrocyte cultures. Cytokine stimulation of NGF mRNA expression by human fetal astrocytes was difficult to assess, possibly due to developmental insensitivity to cytokines or to undetectable levels of NGF mRNA expression at this early stage. Traditionally thought to be an impediment to axonal regeneration or remyelination, reactive gliosis may actually be a physiological attempt at promoting CNS regeneration. The stimulation of astrocyte production of neurotrophic factors by cytokines is an important aspect of this inflammatory process, and warrants further study.

OB1

RETRIEVAL AND QUALITY OF OBSTETRICAL ANAESTHESIA CLINICAL TRIALS: IMPLICATIONS FOR META-ANALYSIS. J.S. Bender BSc.*, S.H. Halpern M.D., M. Thangaroopan BSc., A.R. Jadad M.D., A.Ohlsson M.D. Department of Anaesthesia, Women's College Hospital

INTRODUCTION: Obstetrical Anaesthesia research comprises many small trials and meta-analyses should be feasible on related topics. The purpose of this study was to determine whether randomized trials were easily retrieved using a broad search strategy from MEDLINE and to determine the quality of Obstetrical Anaesthesia studies. METHODS: Randomized controlled trials in obstetrical anaesthesia were collected. These were identified by a broad MEDLINE search and by a handsearch. Included were trials published between January 1985 and December 1994 in ten journals. Each trial was assigned a quality score using a recently available and validated scale (1). This 5 point scale has the following components: randomization, blinding, and description of dropouts. The overall quality of the research was described and compared over time and by journal using the Kruskal-Wallis test ($p < 0.05$ statistically significant). RESULTS: The intraclass correlation coefficient for the quality scale was 0.85. 333 articles were identified and assessed. 176 papers were identified by the MEDLINE search and 157 additional papers were collected in the handsearch. There was a significant difference in the quality scores of the articles between journals and between years. CONCLUSIONS: Care must be taken when applying meta-analytic methods to obstetrical anaesthesia research. Other strategies than a MEDLINE search must be used to retrieve studies since almost 50% will be missed using MEDLINE alone. It has been shown that poor quality papers are more likely to be biased in favor of a new treatment (2). Therefore to increase the reliability of a meta-analysis, sensitivity analyses based on quality should be performed.

REFERENCES:
1) Controlled Clinical Trials 1995; in press 2) JAMA 1994: 272: 125-128

OB2

INDOMETHACIN FOR THE ACUTE TOCOLYSIS OF PRETERM LABOUR: A META-ANALYSIS OF RCTs B. Tan*, K. Panter and M. Hannah. Perinatal Clinical Epidemiology Unit, Women's College Hospital, University of Toronto, Ontario.

OBJECTIVE: To identify all RCTs which have compared Indomethacin with placebo or no treatment for the acute tocolysis (<72hrs) of preterm labour in women with intact membranes and to undertake a meta-analysis of the results.

STUDY DESIGN: The inclusion criteria used to select studies were: randomized controlled trials, women in preterm labour with intact membranes who were treated for ≤ 72 hours. Computer searches of MEDLINE, EMBASE, CDSR, and manual searches of key journals and Society of Perinatal Obstetricians' abstracts were conducted. Data collection forms were constructed with chosen variables relating to delivery delay, maternal side effects, perinatal mortality and neonatal morbidity. Two assessors then abstracted the data independently. Results were pooled and checked for discrepancies. Authors were contacted for additional data. For each outcome variable, a typical odds ratio (OR) and 95% confidence intervals (CI) were calculate using the Peto method in the ORcalc program.

RESULTS: 5 articles were identified, of which 3 met the inclusion criteria. The quality of these articles was high. There was no difference in maternal side effects between the two groups. Perinatal outcomes are reported in the table below:

Perinatal outcomes (*denotes significance)	no.of trials	tot. no. events/ tot. no. entered Indomethacin	Control	typical OR	95% CI low	high
Deliv. Delay <48hrs*	1	1/18	14/18	0.06	0.02	0.21
Preterm Birth <37w*	1	3/18	14/18	0.09	0.03	0.34
Mortality/Stillbirths	3	3/94	4/93	0.70	0.15	3.30
Birthweight <2500g*	2	18/78	36/78	0.36	0.18	0.69
Resp. Distress Synd.	3	5/94	7/93	0.64	0.19	2.21
Bronchopulm. Dyspl.	1	0/16	2/15	0.12	0.01	1.98

CONCLUSIONS: Indomethacin appears to delay delivery delay by 48hrs, to reduce the risk of birthweight <2500g and reduce the risk of preterm birth. These RCTs are too small to assess the effects of indomethacin on maternal side effects, perinatal mortality and neonatal morbidity. This will require larger RCTs.

OB3

IN SITU EXPRESSION OF CONNEXIN-43 mRNA IN PREGNANT RAT UTERI. Grace E. Erb,* Stephen J. Lye, and Neil J. MacLusky. The Department of Reproductive Science, The Toronto Hospital Research Institute, and Depts. of Obstetrics and Gynaecology and of Physiology, University of Toronto.

During pregnancy the uterus is relatively quiescent and unresponsive. With the onset of labor the uterus becomes excitable and capable of extensive cell-to-cell coordination. Such coordination is required for labour-associated contractions and consequently birth. Intercellular gap junctions provide direct physical contact between adjacent cells. Thus, between myometrial cells gap junctions can provide communication pathways for the coordination of tissue responses. One of the important gap junction proteins synthesized during labour is connexin-43 (Cx-43). In rat uteri Cx-43 mRNA, protein and gap junctional area increase near term. Localization of these responses within uterine tissue, however, is poorly understood. In an attempt to resolve this issue, rat uteri around the time of labour were examined. Uteri were obtained from rats on days 21, 22, 23 (during labour), and one day post partum. To establish the hormonal dependence of changes in Cx-43 expression, these tissue samples were compared to uteri removed from ovariectomized (OVX) rats killed after administration of estrogen and/or progesterone. *In situ* hybridization techniques were used to examine the distribution of Cx-43 gene expression in uterine tissue sections. Increased levels of Cx-43 mRNA were observed in the pregnant uteri close to the time of labour and delivery, as well as in estrogen-treated but not progesterone-treated OVX rat uteri. These results are consistent with previous data indicating that Cx-43 gene expression is enhanced close to term. Unexpectedly, however, although it is known that essentially all myometrial cells are estrogen receptor-positive, increased Cx-43 expression in the myometrium appeared to be markedly heterogeneous. Thus, in the estrogen-treated uteri, only about 30% of the myometrial cells present in the circular uterine muscle layer displayed significant Cx-43 mRNA expression. These results raise the possibility that increased gap junctional communication in the estrogen-treated OVX or pregnant rat uterus may be co-ordinated by a sub-set of myometrial cells that have a specific capacity to respond to rising estrogen levels through increased Cx-43 biosynthesis.

ON1

ALTERATIONS OF THE CELL CYCLE CAUSED BY A NOVEL FAMILY OF ANTINEOPLASTIC AGENTS. J. Pressacco*, P. Poyet, J. Lacroix, and R. C.-Gaudreault. Département de la Recherche, Hôpital St.-François D'Assise, Québec, Canada G1L 3L5.

A novel family of anticancer agents, 1-aryl-3-(2-chloroethyl) urea derivatives, was developed by this laboratory. These agents exhibit potent pharmacological properties both *in vitro* and *in vivo*. Studies with the active 4-tert-butyl derivative (tBCEU) demonstrated tremendous antineoplastic activity on many different tumour cell lines including some resistant lines. The antineoplastic effect of tBCEU is proposed to be, in part, caused by an alteration of tubulin and vimentin synthesis. In this study we attempt to determine the effects of these novel drugs on the cell cycle of a non-hormonal dependent human breast cancer cell line, MDA-MB-231, using flow cytometric analysis. Cellular DNA was labelled with propidium iodide and analyzed using an Epics Analyzer Flow Cytometer equipped with an air cooled argon laser emitting at 488 nm. Fluorescence was then detected of at least 2 x 10^4 cells for each sample at 640 $\pm$ 20 nm. Three drugs, including tBCEU, from this family of urea derivatives were investigated. With all the drugs, increasing time of exposure and/or increasing drug concentrations produced a decrease in the G_0/G_1 peak and a distinct broadening of the G_2/M peak, consistent with an arrest in M-phase. Combining results from previous studies to those obtained here, there is a strong suggestion that the mechanism of cytotoxicity of these novel drugs is through an alteration of tubulin and vimentin synthesis leading to an M-phase cell cycle arrest.

This project was made possible by the Leukemia Foundation - Ethel London Memorial Fund.

ON2

Early Screening for Ovarian Cancer in Pre-symptomatic Women at High Risk: Looking for serum anti-p53 antibodies. K.A. Gronau*, B.P.Rosen[1], K.J. Murphy[1], E.P. Diamandis[3] and D.E.C. Cole[2,3] Depts. of [1]Obstetrics/ Gynecology, [2]Medicine, & [3]Clin. Biochem., Univ. of Toronto, Toronto, ON M5S 1A8, Canada.

Ovarian cancer is the most prevalent lethal gynecological cancer. Although the etiology of this disease is complex and poorly understood, certain predictors of risk have been established, the strongest of which is a positive family history (16% of affected women). Early diagnosis of ovarian cancer is important, as survival is much decreased if diagnosed at a late stage. Currently, at-risk women with strong family histories can be screened for the tumour marker CA125. In affected or asymptomatic women, a positive screen is reliably related to significant tumour burden. The tumour-suppressor gene p53 is an oncogene often implicated in ovarian cancer. Many malignant ovarian tumours produce mutant p53, and p53 germ-line mutations have been found in 10-16% of ovarian cancers in one series. In another study, antibodies against p53 (p53ab) were found in 15% of non-familial ovarian cancer patients. Because of the strong predictive value of a positive family history of ovarian cancer and the unknown incidence of serum p53ab in familial ovarian cancer patients, we decided to determine whether screening unaffected family members for p53ab is potentially useful in early detection. 162 asymptomatic women and 14 women with breast or ovarian cancer in high-risk families from the Toronto Hospital Familial Ovarian Cancer Clinic were screened for p53ab. Patient serum was added to microtiter strips coated with wild-type p53 protein. Alkaline phosphatase-labelled goat anti-human IgG (ALP-IgG) was then added, and activated by a standard fluorescence developing system. Fluorescence greater than twice background was considered positive. Only samples containing p53ab bind both the plate and the ALP-IgG and therefore fluoresce. As expected, 2/14 affected women tested positive for the antibodies (14%). Importantly, 2/162 (1.3%) *unaffected* women also tested positive. Only one had an elevated CA125. Thus, it is possible that this blood test for p53ab may have the potential for use as an early predictor of cancer predisposition in women at high risk because of their family history.

ON3

LONG TERM SURVIVAL FOLLOWING PERCUTANEOUS TRANSHEPATIC DRAINAGE - A RETROSPECTIVE STUDY. Amit Mehta*, C.S.HO. Department of Radiology, The Toronto Hospital - General Division. Toronto, Ontario, Canada.

Purpose: Proximal biliary tract cancer carries a dismal prognosis. Three methods of treatment for preoperative decompression and for palliation in obstructive jaundice exist; these are surgical, endoscopic stent and percutaneous transhepatic biliary drainage (PTCD). Statistics on long term survival are available for surgical and endoscopic treatments, but are lacking for PTCD. This study evaluates the long term survival experience for individuals with proximal biliary duct carcinoma termed Klatskin tumors.
Materials and Methods: Chart review was conducted on 68 patients who were diagnosed with Klatskin tumors between 1983 and 1994. These patients were categorized into primary carcinomas and metastatic or secondary carcinoma with subsequent review ensuring that no previous therapy had been conducted. Survival was measured and the results analyzed with a Kaplan-Meier survival plot using SPSS 6.0 PC software.
Results: Preliminary results indicate a significant extension in the length of survival in patients treated with PTCD. Patients with primary carcinoma of the proximal duct show a mean survival time of 14.20 months and a median of 8.67 months. Patients with secondary carcinoma show a mean survival time of 6.44 months and a median of 4.03 months.
Conclusions: PTCD is an effective means of palliation in patients with Klatskin tumors. Long term survival is significantly higher in those patients with primary cancer as compared to those with metastatic disease. PTCD shows significantly longer survival times than other methods of treatment currently employed in treating proximal duct carcinoma.

ON4

MANAGEMENT OF THYROID NODULARITY IN THE PREGNANT STATE. M.J. Korman*, D. Farine, P.G. Walfish, I.B. Rosen. Mt. Sinai Hospital, Toronto, Ontario, Canada M5G 1X5.

Thyroid nodularity during pregnancy has been commonly ascribed to benign hyperplasia. There is a relative paucity of reported cases of thyroid cancer in pregnancy and conflicting attitudes exist regarding management. Forty-seven women ranging in age from 20 to 40 presented for assessment and management, 43 with solitary nodules, 4 with multinodular disease, 25 underwent thyroid feeding which was ineffective. Three underwent operation in mid-trimester, the rest at postpartum period. Operation consisted of total thyroidectomy and appropriate neck dissection. Neoplasia was encountered in 80% of 47 patients. Nodal involvement occurred in 3/47, exposure to radiation occurred in 2/47. In 20 cases of malignancy, FNAB could be assessed showing 3 false negatives. In 16 adenoma cases, 15 were correctly diagnosed. Aggravation of tumor growth was seen in 7/47. Followup varied from 0 to 15 years with no incidence of recurrence or metastases. Four patients underwent surgery elsewhere. One patient has been lost to followup and 1 patient presented with Graves's associated neoplasia. Conclusions indicate that (1) thyroid nodularity in pregnancy in North America should be assessed with a view to excluding neoplasia, (2) pregnancy may be tumor antagonistic and that heightened physician consciousness is warranted, (3) management of thyroid nodularity demands FNAB. If negative for CA, excision can be delayed until the postpartum period; if positive, resection can be carried out in mid-trimester. Course of cancer neoplasia has generally been unaggressive.

ON5

COMPARISON OF CONVENTIONAL PAP SMEARS, THINPREP™ SMEARS AND BIOPSIES IN THE DIAGNOSIS OF CERVICAL LESIONS. Kosta Milankov*, Y.C. Bedard and J.B.M. Mullen. Department of Pathology, Mount Sinai Hospital and Faculty of Medicine, University of Toronto, Toronto, Canada, M5S 1A8.

In this study, the accuracy of conventional Pap smear (CS) and ThinPrep™ Processor smear (TPS) diagnoses were compared to Biopsies (BIOP), considered as the *gold standard* for diagnostic accuracy, where applicable. When compared together, CS and TPS diagnoses had an exact agreement in 863 of the 912 cases (94.6%). In the assessment for agreement and accuracy, CS diagnoses agreed exactly with BIOP diagnoses in 73 of the 147 cases (49.7%). The CS was found to have a sensitivity of 76.6%, specificity of 73.8%, false-negative rate of 23.4%, false-positive rate of 26.2%, positive predictive value of 81.7% and a negative predictive value of 67.4% when correlated to the BIOP. In the assessment of agreement and accuracy of TPS diagnoses with BIOP diagnoses, TPS was found to be in exact agreement with BIOP results in 67 of the 147 cases (45.6%). Comparison of TPS diagnoses to BIOP diagnoses revealed similar values for TPS sensitivity (71.4%), specificity (73.8%), false-negative rate (28.6%), false-positive rate (26.2%), positive predictive value (80.4%) and negative predictive value (63.6%). Furthermore, the CS had the same rate of missed diagnoses when compared to the BIOP (21 and 19 cases, respectively) which was similar to the rate of missed diagnoses encountered when CS and TPS diagnoses were compared (20 cases each). However, when TPS and BIOP diagnoses were compared, the TPS had a higher rate of missed diagnoses compared to the BIOP (27 cases compared to 19 cases, respectively). The results presented herein show that although the CS was slightly more accurate than the TPS when compared to the BIOP, this difference was not statistically significant, indicating that the CS and TPS are equal in diagnostic power in the detection of cervical lesions.

ON6

THE ADEQUACY OF PAP SMEAR SCREENING AND ITS ROLE IN THE DEVELOPMENT OF CERVICAL CANCER N. A. Cherry*, Dr. R Osborne, Dr. P. Shaw, and Dr. A. Clarke. Dept. of Gynecologic Oncology, T-SRCC, Toronto, Ontario, M4N 3M5

Cervical cancer has been called a preventable disease by the National Cancer Institute (N C.I.) In addition, it is perhaps the best example of a medical condition for which there exists a safe, inexpensive screening tool which has demonstrated efficacy. There is ample retrospective evidence that Pap Smear Screening provides early detection of pre-clinical disease and thereby prevents the development of invasive cervical cancer. Why then are women still developing cancer of the cervix?

A retrospective chart review was conducted on 197 patients referred to the Toronto Sunnybrook Regional Cancer Center with a referral diagnosis of invasive cervical cancer. Additional information was also obtained from patient interviews and referring and family physicians' records. The study extended from January 1993 to December 1994 All pathology was reviewed. The chart review showed that of the 197 patients, 36 (19%) had had a pap smear within 12 months prior to diagnosis, 37 (19%) had had a cervical cytology 12-36 months prior to diagnosis, 57 (30%) had either not had a pap smear within 36 months or had never had a pap smear, and the remaining 64 (33%) had no record of previous pap smears in their charts

These findings indicate that a large proportion of women who are still developing cervical cancer are not being adequately screened. This study demonstrates the need for a centralized cytologic screening program with recall capability

ON7

EXPRESSION OF THE PROTEOGLYCAN, OCI-5, IS REGULATED BY CELL SHAPE IN INTESTINAL CELLS. M. Li*, R.N. Buick. Department of Medical Biophysics, Ontario Cancer Institute/Princess Margaret Hospital, University of Toronto, Toronto, Canada.

OCI-5 is a member of the glypican-related integral membrane proteoglycan (GRIP) family, and is believed to function during development and/or differentiation of the intestinal epithelium. In the fetal rat intestine, the OCI-5 transcript is transiently expressed at high levels during a period of rapid cellular proliferation, differentiation and morphogenesis. To investigate the mechanism of its regulation during intestinal development, OCI-5 expression was studied in the primitive rat intestinal epithelial cell line, IEC-18. The transcription of OCI-5 was previously shown to be highly induced in IEC-18 at confluence. Neither serum deprivation nor experiments switching conditioned media/basement membrane between confluent and growing cells induces OCI-5. Culture of IEC-18 in low calcium media disrupts cell-cell contacts, resulting in a more rounded cellular appearance, and an induction of the OCI-5 transcript. Similarly, culture of IEC-18 on dishes coated with polyHEMA, a substrate to which cells can adhere but not spread, increases OCI-5 expression. Cytoskeletal disruption with non-toxic doses of colchicine reduces the levels of OCI-5 in confluent IEC-18. In addition, treatment of cells with vanadate, a general phosphatase inhibitor, abolishes the confluent-dependent activation of OCI-5. These data suggest that OCI-5 expression is regulated in IEC-18 by cell shape, utilizing a pathway involving tyrosine de-phosphorylation. The confluent state of IEC-18 results in a highly compacted cellular architecture, perhaps mimicking the compaction, re-ordering and migration of cells during intestinal morphogenesis. A role for cell shape in regulating gene expression during development is intuitively attractive and increasingly recognized.

ON8

THE PERCEIVED INFORMATION NEEDS OF BREAST CANCER PATIENTS. T. Mark*, M. Trudeau, J. Blondal, L. Lickley. Henrietta Banting Breast Centre, Women's College Hospital, Toronto, ON, M5S IB6.

Each year, approximately 17,000 Canadian women are diagnosed with breast cancer. In order to better provide these women with the information that they need to deal with their illness, it is necessary to learn what their perceived information needs are at the time of their appointment with the medical oncologist and how they feel their needs can best be met. The purpose of this study was to develop and test a set of Pre-Consultation and Post-Consultation descriptional questionnaire surveys asking women with a first-time diagnosis of breast cancer and seeing the medical oncologist for the first time post-surgery to indicate what information topics are important to them, their level of satisfaction with the information being received during the consultation, and ways to improve the information sharing process. Information was gathered from ten complete sets of Pre- and Post-Consultation questionnaires. The results of this study show that these women do have specific information needs. For the majority of given topics regarding the nature of the disease, treatment, etc., this group of women felt that the information shared by the oncologist was important to them, useful, understandable, and capable of being remembered. Some areas where subjects felt there was a need for more information included lifestyle changes and diet. This group of women wanted as much information as possible and wanted to be involved with the decisions about their medical care. All of them felt that they learn best from a variety of resources. This test study gathered suggestions about how to facilitate the information sharing process between doctor and patient. As well, areas were identified for improving the questionnaires so that they may be self-administered in the future in order to gather more information about the perceived information needs of women with breast cancer.

ON9

IMMUNOHISTOCHEMICAL ASSAY OF ESTROGEN RECEPTORS ON CYTOLOGIC AND HISTOLOGIC SAMPLES OF BREAST CARCINOMA. D. Gorman*, L. Orcheson°, L. Thompson°, P. Goss†¶ and S. Boerner†¶. The Departments of Nutritional Sciences°, Medicine‡ and Pathology†, University of Toronto, Toronto, ON, M5S 1A8 and The Toronto Hospital¶, Toronto, ON, M5G 2C4.

Immunohistochemical (IHC) detection of estrogen receptor (ER) expression in paraffin-embedded fine needle aspirates (FNA) of breast carcinoma was compared to detection in histologic sections and biochemical assays of fresh tumour. It was hypothesized that a good correlation would exist between the immunoscore of the FNA and histologic sections, and that both of these would correlate with the level of ER determined by biochemical methods.

ER analysis was performed by monoclonal antibody immunoperoxidase techniques on paraffin-embedded preoperative FNA and surgically excised breast carcinomas from seventeen pre- and post-menopausal women with palpable breast carcinomas. The results of the immunohistochemistry were quantitated by a visual scoring system. Biochemical determination of ER content was performed by dextran coated charcoal (DCC) assay on snap-frozen samples of the tumours obtained at the time of excision.

Fourteen of the 17 cytologic samples and all 17 histologic samples were evaluable by IHC with biochemical results available on 12 cases. A significant correlation was found between the ER content by DCC and the immunoscores of the FNA (coefficient of correlation [r] = 0.885, $p < 0.0001$) and histology ($r = 0.539$, $p < 0.067$). A significant correlation was also found between the FNA and histology immunoscores ($r = 0.661$, $p < 0.010$). Discrepancies between cytology and histology immunoscores seem to arise from sampling error due to the endogenous heterogeneity of expression of ER by the tumours.

It is possible to accurately determine ER expression in paraffin-embedded FNA of breast carcinoma by immunohistochemical analysis with comparable results to IHC analysis of the excised tumour and ER content determined by traditional biochemical methods. ER analysis by IHC on FNA of breast carcinoma may eliminate the need for open biopsy to determine ER status. IHC assay for ER could be used to study the effects of various agents on estrogen receptor expresion of tumours by obtaining a pretreatment FNA for ER analysis followed by a post-treatment ER content determined on repeat FNA or on the excised tumour.

OPHTHALMOLOGY

OP1

ENDOPHTHALMITIS FOLLOWING CATARACT EXTRACTION: A COMPARISON OF EXTRACAPSULAR AND PHACOEMULSIFICATION. S. Somani*, A. Grinbaum MD, A. Slomovic MD. The Department of Ophthalmology, Toronto Hospital, Western Division.

Purpose: To compare the incidence, clinical presentation, pathogens and outcome of endophthalmitis following cataract extraction using the extracapsular and phacoemulsification techniques.

Material and Methods: The medical records of patients with culture-positive endophthalmitis over a 6 year period following extracapsular (n=60) and phacoemulsification (n=15) cataract extraction were retrospectively reviewed.

Results: There was no significant difference in the incidence of endophthalmitis following extracapsular cataract extraction and that following phacoemulsification, 0.31% vs 0.30% (Chi=0.002). Both groups were found to have similar clinical presentation of endophthalmitis. The median time from surgery to presentation was also similar following the two techniques, 5 days vs 6 days. The most common pathogen isolated in both groups was coagulase-negative Staphylococcus, accounting for 62% of the cases following extracapsular and 67% following phacoemulsification. A similar visual outcome was also found between both groups, with a vision of 20/50 or better being achieved in 38% of extracapsular cases and 33% of phacoemulsification cases. A vision of 20/400 or worse was found in 31%, and 33% of the cases respectively.

Conclusions: Despite the differences in the surgical technique of extracapsular cataract extraction and phacoemulsification, the clinical spectrum of endophthalmitis appears to be similar. This may indicate that there is no correlation between the occurance and severity of endophthalmitis and the nature of the surgical technique used.

OP2

THE HORIZONTAL VESTIBULO-OCULAR REFLEX GAIN DURING ACTIVE AND PASSIVE HEAD ON BODY ROTATIONS. M.C. Hartleib*, N. Torun, and J.A. Sharpe. Division. of Neurology, The Toronto Hospital.

The vestibulo-ocular reflex (VOR) preserves vision during head rotations by stabilizing the eyes in space relative to the visual scene. To maintain clear and stable vision the gain of the VOR (the ratio of eye velocity to head velocity) must approach -1.0, thus stabilizing the target image on the retina. Vestibular signals may be only one of a number of inputs which converge upon a larger multicomponent gaze control center whose final goal is to compensate for head movement by utilizing all available information. Both visual and non-visual cues would be expected to alter the gain of the VOR. A difference might be expected to exist between VOR gains for self generated head movements compared to passively generated rotations if non-visual influences had a significant effect on VOR gain. For example during a self generated head movement, VOR pathways may be modified by knowledge of the nature of the forthcoming movement (prediction) and/or an efference motor copy (pre-programming) of the commands to neck musculature. This study compared the VOR gain of active (self generated) vs. passive (generated by the examiner) sinusoidal head on body rotation and/or impulsive non-predictable head on body rotations in seven subjects in order to determine the roles of non visual modulating subsystems on the reflex. No significant differences were found between the VOR gains of actively and passively generated sinusoidal head on body rotations in either the dark or the light. However, the gain of actively generated impulsive head rotations was significantly higher than passively generated non-predictable head rotations in both the light and the dark. These data support the hypothesis that prediction affects VOR gain. The data are consistent with the hypothesis that non-visual influences, specifically prediction, can enhance VOR gain.

PAEDIATRICS

P1

PEDIATRIC HEART SURGERY: ARE ELEVATED SERUM FREE FATTY ACIDS (FFA) DETRIMENTAL TO THE HEART? N. Wong*, V. de Souza, J. Coles, W. Williams, P. St Louis, C. Wittnich. Division of Cardiovascular Surgery, Hospital For Sick Children, Department of Surgery, University of Toronto, Toronto, On., M5S 1A8

In adults, high dose heparin administration increases FFA levels and is associated with post-ischemic arrhythmias and decreased ventricular function. We have previously demonstrated that children also have elevated FFA levels in response to heparin administration. **Objectives**: *(a)* To determine whether elevations in serum FFA adversely affects myocardial performance in children undergoing cardiopulmonary bypass (CPB). *(b)* Identify risk factors which may exacerbate any detrimental effects of elevated serum FFA. **Methods**: In 29 children ranging in age from 2 days to 18 years (13 males, 16 females) FFA was measured prior to heparin (pre-hep), 10 min. after heparin administration (on CPB), and 5 min. post-protamine (to reverse heparin effects). A retrospective analysis was done on the following data: age, gender, blood gases and myocardial function (wall motion via transesophageal echocardiography). Depressed post-operative myocardial performance was indicated if three of the following indices were met: arrhythmias post-op, fibrillation post-op, use of mechanical hemodynamic support (ECMO), use of inotropes, or decreased ventricular function. **Results**: *(a)* FFA levels (mean±SD; mM) were: 0.81±0.40 pre-hep; 1.37±0.52 post-hep; and 0.87±0.48 post-protamine. Patients were classified as having "elevated" FFA levels if they had a value ≥ 1.0 mM at any sample interval. 83% of patients had elevated FFA at any sample interval and in 10 of these 24 patients, this was irrespective of heparin administration. All patients who experienced decreased heart function had elevated FFA. In patients with prolonged ischemia due to extended aortic cross clamp (AXC) times, 67% had decreased heart function post-op. All of these patients also had elevated FFA. Interestingly, patients without AXC (no ischemia), who also had elevated FFA, did not have decreased heart function. *(b)* In twelve patients that were cyanotic pre-op, all but one had elevated FFA, and 67% also had decreased heart function. All cyanotics who had decreased heart function also had elevated FFA. **Conclusions**: In children, heparin administration results in elevated FFA levels. Patients with prolonged AXC and FFA levels ≥ 1mM had decreased heart function. Cyanosis exacerbates the deleterious effects of elevated FFA.

PHARMACOLOGY AND PHYSIOLOGY

PH1

COUPLING OF PARATHYROID HORMONE RECEPTORS TO ADENYLYL CYCLASE ACTIVATION IS CELL CYCLE DEPENDENT. J. Sarjeant* and J. Mitchell Dept. of Pharmacology, University of Toronto, Toronto, Ontario, M5S 1A8.

The UMR 106 clonal osteosarcoma cell line has been extensively used as a model of osseous PTH target cells. We have previously reported three morphologically distinguishable cell types in this cell line and demonstrated the majority of PTH receptor expression on one of these cells. We have suggested that this is the result of cell cycle-dependent expression of PTH receptors in osteoblastic cells. To test this hypothesis in this study we have synchronized UMR 106 cell cultures in GO/G1 phase of the cell cycle by a combination of serum deprivation and pertussis toxin treatment. Cells were then allowed to progress through the cell cycle following addition of serum. Our results demonstrate that GO/G1 arrested cells progress to the peak of S phase during the first 21 hours after addition of serum as assessed by ^{3}H-thymidine incorporation into DNA. During the next 6 hours cells progress into G2/M phase of the cell cycle and subsequently back into G1 after 30 hours. We then examined the cells response to PTH during GO/G1, S and G2/M phase at 6, 21 and 27 hours after serum stimulation. Our results demonstrate that cells in GO/G1 phase show the greatest PTH stimulation of adenylyl cyclase, with four fold higher maximal response than that seen in S phase cells and two fold higher than in G2/M phase cells. These results, in addition to our previous work, demonstrate that PTH receptors coupled to adenylyl cyclase are predominant in resting osteoblastic cells. Others have shown that PTH coupling to intracellular Ca^{2+} predominates in cells UMR cells in S phase. Together these results provide an experimental model for the study of endogenous and therapeutic factors that can influence osteoblasts to either stimulate bone resorption or bone deposition.

PH2

THE EFFECTS OF NEGATIVE PRESSURE BREATHING ON RESPONSES TO SIMPLE TESTS OF AUTONOMIC FUNCTION. K.L. Barker*, M. Marantz, J. Sharp-Kehl and J.R. Ledsome. Dept. of Physiology, U.B.C., Vancouver, B.C., V6T 1Z3

Physiological consequences of weightlessness and cardiovascular abnormalities that occur on return from space may be due in part to changes in function of the autonomic nervous system (ANS). Negative pressure breathing (NPB) causes an acute shift in blood volume to the thoracic cavity similar to that seen during spaceflight. However, we have been unable to identify any previous studies of the effects of NPB on tests of ANS function. Our hypothesis was that NPB would reduce the mean arterial pressure (MAP) and heart rate (HR) responses to two standard tests of ANS function, isometric exercise (ISO) and the cold pressor test (CPT). In this study, ISO and the CPT were performed on 13 volunteers during ambient pressure breathing (APB) and NPB. MAP and HR responses to ISO were not attenuated by NPB. In contrast, NPB significantly attenuated the BP and HR responses to the CPT. NPB caused an increase in MAP of 14.8 mmHg compared to an increase of 17.7 mmHg during APB, and an increase in HR of 3.8 beats/min compared to an increase of 7.2 beats/min during APB. In conclusion, NPB attenuates the increases in MAP and HR that occur in response to the CPT and does not alter MAP and HR responses to ISO. This study also demonstrates the feasibility of using NPB as a simulation for the acute changes in blood volume that occur in microgravity.

PHARMACOLOGY AND PHYSIOLOGY

PH3

PULMONARY VOLUME-RELATED FEEDBACK ANTAGONIZES TRACHEAL TONE ABOVE THE APNEIC THRESHOLD. J.A. Silverman*, L.Z. Sommer, S. Iscoe, and J.A. Fisher. Department of Anaesthesia, Mount Sinai Hospital, University of Toronto, Toronto, ON M5G 1X5

Although tracheal tone (TT) is related to phasic inspiratory (phrenic) activity, we showed, using a new sensitive technique to measure tracheal diameter, that most of the tracheal constriction occurs at a $PaCO_2$ when phrenic activity was absent (i.e., below the apneic threshold, AT). Nevertheless, we hypothesized that TT would increase with respiratory drive even after maximal constriction of the trachea is attained. Because it is difficult to measure directly TT above AT, we deduced the level of TT by measuring the effect on tracheal diameter of pulmonary slowly adapting receptor (SAR) feedback, an input known to cause tracheal dilatation. In 6 pentobarbital-anesthetized, intubated, paralyzed, and ventilated dogs, we measured changes in tracheal diameter in response to increases in SAR input. We applied step increases in tidal volume and frequency while keeping $PaCO_2$ constant, both above and below the AT. Above AT, increases in tidal volume caused significantly less tracheal constriction ($p < 0.05$, paired *t* test) than the same increase in volume below AT. Increases in ventilator frequency did not affect tracheal diameter above or below AT. We interpret the reduced effect of SAR input above AT as indicating that TT continued to increase even after tracheal constriction was maximal.

PH4

THE ROLE OF GLUTATHIONE S-TRANSFERASE ISOZYMES IN THE RESISTANCE OF HUMAN COLON CANCER CELL LINES TO DOXORUBICIN K. Ahmad*, P.O. Beaumont, M.J. Moore and D.S. Riddick. Depts. of Pharmacology and Medicine, University of Toronto, Toronto, ON., M5S 1A8

Colorectal cancer is the second leading cause of cancer deaths in North America due, in part, to a high incidence of intrinsic drug resistance. Doxorubicin, a commonly used anthracycline, is effective in many types of cancer but has little activity against colorectal cancers. It is hypothesized that this is due to a multifactorial resistance mechanism in which the glutathione S-transferase (GST)-glutathione (GSH) enzyme-cofactor system plays a role. Our objective was to examine the relationship between GST isozyme expression and doxorubicin resistance in four human colon adenocarcinoma cell lines (CaCo-2, LoVo, HT-29 and SW620), so as to provide a basis for studies of drug resistance modulation by GST inhibitors. GST catalytic activity was measured by spectrophotometric assay, using general and isozyme-selective substrates, and GST protein expression was assessed by immunoblot. The sensitivity of the cell lines to doxorubicin was determined using a microplate colorimetric cytotoxicity assay.

Total GST activity was measured as the rate of conjugation of 1-chloro-2,4-dinitrobenzene (CDNB) with GSH and was significantly higher in CaCo-2 cells ($p < 0.001$) as compared to the other cell lines. The four cell lines did not differ in GST-π immunoreactive protein or GST-π selective catalytic activity as assessed by ethacrynic acid-GSH conjugation. Preliminary results also show a unique GST-α immunoreactive band in CaCo-2 cells, not present in the other cell lines. CaCo-2 cells were most resistant to doxorubicin, showing an IC_{50} value approximately 10-fold higher than LoVo and HT-29 and 100-fold higher than SW620.

These results will help to elucidate the relationship between GST expression and drug resistance, as well as directing ongoing studies in modulating doxorubicin resistance with the use of isozyme-selective GST inhibitors. The ultimate goal of this project is to conduct clinical trials of doxorubicin with a GST enzyme inhibitor in colorectal cancer patients.

PSYCHOLOGY AND PSYCHIATRY

PS1

QUALITY OF LIFE IN LIVER TRANSPLANT RECIPIENTS M. Silverberg*, S. Abbey, M. Pearce, P. Greig and G. Levy. Liver Transplant Program, The Toronto Hospital, Toronto, Ont., M5G 2C4. This study tested the hypothesis that depression was correlated with poor quality of life in liver transplant recipients, and explored the possible contributions of other factors. 52 liver transplant recipients (31 male, 21 female), aged 25 to 67, were interviewed using a structured Clinical Interview for Diagnoses (SCID) for depression and mania and completed a questionnaire containing self-report measures of depressive symptomatology, disease specific and disease generic quality of life measures, measures of optimism, and measures of illness intrusiveness into 13 life domains. Demographics, post-transplant complications, and current medications were obtained from patient charts.

Preliminary results indicate self-reported depressive symptoms of mild to moderate severity in 34.2% of the sample, of moderate severity in 7.9%, and a current diagnosis of major depression in 7.8% of the sample. 21.6% of participants have a past history of mood changes after transplantation. There is a relationship between depressive symptomatology and poor quality of life as measured by the Liver Disease Specific Quality of Life Quesionnaire. Depression may be an indicator of poor quality of life in liver transplant patients.

PS2

THE EFFECT OF AGE AND AGE OF ONSET ON DEPRESSIVE ILLNESS. A. ORDEAN* BSc., N. HERRMANN MD, FRCP(C) . Sunnybrook Health Science Centre, Toronto, Ontario, M4N 3M5.

This study attempted to determine whether individuals developing depression for the first time in early life are different from those developing this illness in later life. A retrospective chart review of 247 first-time admissions to a geriatric psychiatric inpatient unit was undertaken. The inclusion criteria for the study included a.) age greater than 65 years at index admission, b.)inpatient status, and c.)index hospitalization after 1982. Of the charts reviewed, 145 were diagnosed with affective disorders and were further studied. Information was obtained from all available sources including physicians' admission notes, discharge summaries and social work records.

Preliminary data of the analysis planned has shown no correlation between age and length of hospitalization, the presence of psychosis, the presence of cognitive impairment, positive family history, response to treatment or outcome following ECT treatment.

Using a cut-off age of 60 years to analyze the data based on first admission, three groups were identified: EO(first admission < 60), LO(first admission >= 60) and FAIH(first admission is index hospitalization). The preliminary data analysis revealed a statistical difference for the average age of first admission for the three groups. No significant difference was found for age of onset and length of stay, marital status, living situation and housing situation. If differences do exist, this could significantly influence the prognosis and the modes of therapy for depressive illnesses.

PS3

PLASMA INTERLEUKIN-1 RECEPTOR ANTAGONIST & INTERLEUKIN-1ß DURING NOCTURNAL SLEEP IN YOUNG MEN. D Liu*, CG Jiang, LA Lue, H Moldofsky, RM Gorczynski. The Toronto Hospital, Western Division, Center for Sleep & Chronobiology, Toronto.

Previous studies demonstrate that Interleukin-1 (IL-1) promotes slow wave sleep (SWS) in animal models. In addition, higher IL-1-like activity is found in humans during SWS. Because the IL-1 Receptor Antagonist (IL-1ra) has been shown to block the actions of IL-1ß induced shock and SWS activity, a possible homeostatic role for IL-1ra may exist in nocturnal sleep in humans. It has been hypothesized that IL-1ra will be associated with periods of wakefulness in nocturnal sleep.

Eleven healthy males (mean age 24.4) with regular sleep-wake habits were subjected to 5mL serial venous blood samples throughout one night of uneventful sleep. In addition, polysomnographic monitoring was performed with subsequent interpretation of the sleep stages in 30 second epochs. Assays were performed on the venous samples for IL-1ra, IL-1ß (via ELISA method) and cortisol levels (via RIA method). Samples were correlated into hourly means and analyzed using repeated measure ANOVA by time and sleep stage. Significant differences were examined by contrast test.

Pulsitile IL-1ra measure (of 3 to 5x baseline values and statistical significance) were observed in 8 of the 11 subjects. All 8 of these subjects had episodes of nocturnal wakefulness within 5 minutes of the IL-1ra pulse. Seven of the 8 IL-1ra peaks had occurred during the period of minimal cortisol secretion. No correlations were found between IL-1ra and IL-1ß.

The fact that large nocturnal pulses of plasma IL-1ra were associated with periods of wakefulness are consistent with the notion that IL-1ra inhibits IL-1ß sleep in animal models. However, the lack of correlation between IL-1ra and IL-1ß may be a result of the reportedly short half life of endogenously produced IL-1ra. It is worth note that the IL-1ra pulses are more likely to occur during the nocturnal trough of cortisol secretion (possibly suggesting a circadian rhythm), but were largely unrelated to sleep time, sleep stages or IL-1ß.

R1

REDUCING NOISE IN FUNCTIONAL MRI BY ALIGNING IMAGES PRIOR TO BRAIN ACTIVATION MAPPING. M. G. Ossip*, A. Kassam, and M. Wood. Dept. of Medical Imaging, Faculty of Med., Univ. of Toronto, Toronto, M5B 1W8.

Functional magnetic resonance imaging (fMRI) provides information associated with brain activation. Images of a particular anatomical slice are acquired repetitively under the presence of a stimulus and under control conditions. Typical stimuli include vision, smell and pain. According to an established model, the activated regions of the brain are brighter in the images acquired during presentation of the stimulus. Various statistical methods are used to bring out the slight intensity differences. Statistical processing produces an activation map of the brain in which brighter pixels represent activated regions. This processing assumes that the differences between images are due only to brain activation. The main difficulty in fMRI is that any movement during image acquisition creates differences between images due to anatomical misalignment and not brain activation.

The hypothesis was that aligning images prior to statistical processing reduces extraneous variation caused by misalignment, resulting in activation maps containing less noise. The functional magnetic resonance (fmr) images used were acquired by previous investigators. In order to verify that these images were misaligned, they were rapidly displayed in sequential order producing an animation which demonstrated movement. Additionally, the differences between images was quantified confirming the movement observed in the animation. An algorithm was developed to align the images, and it successfully detected and corrected sets of purposely misaligned images. The uncorrected fmr images were processed resulting in brain activation maps obscured by noise. The fmr images were then aligned using the algorithm and reprocessed, resulting in brain activation maps with markedly reduced noise.

These experiments confirmed that misaligned fmr images are routinely obtained in practice, and that aligning them prior to processing produces activation maps which better represent stimulus induced brain activation.

R2

MRI QUANTIFICATION OF CARDIAC IRON IN SECONDARY HEMOCHROMATOSIS. T.N. Sheth*, M. Iwanoschko, W. Kucharczyk, N. Oliveri, P. P. Liu. Centre for Cardiovascular Research, The Toronto Hospital.

Secondary hemochromatosis results from transfusional iron overload in patients with beta-thalassemia. Iron deposition occurs in the heart and liver, commonly leading to death at an early age from precipitous heart failure. Serum ferritin is useful as an initial confirmatory test of iron overload. However, to precisely localize iron in the heart, magnetic resonance imaging (MRI) is most promising. Our group has shown that MRI derived parameters correlate well with tissue iron levels and are the best predictors of prognosis in this population. The aim of the present study is to determine (1) if MRI measurements of cardiac and liver iron content are reproducible over time and (2) whether there is a predictable pattern of iron deposition in these organs.

Methods: 30 patients with serial MRIs, 1 year $^{+}$/- 1 month apart with no change in therapy or clinical status, were randomly selected from a database of patients undergoing regular monitoring at the Toronto Hospital. A two-way, mixed effects intraclass correlation coefficient was used as a measure of agreement.

Results: The agreement between MRIs at 1 year intervals for signal intensity of the heart was found to be good at 0.84, 95% CI (0.73,0.91) and for the liver was found to be excellent at 0.96, 95% CI (0.93, 0.98). MRI-derived parameters of cardiac iron (mean = 0.956) and liver iron (mean = 0.280) were significantly different overall ($p<0.01$) and there was no relationship between iron content in the heart and in the liver in individual patients, Pearson's Coefficient = - 0.12.

Conclusion: MRI quantification of tissue iron levels yields measurements that are reproducible over time and thus MRI is a reliable measure of disease progression and changes due to intervention. Given the substantial individual variation in organ-specific deposition of iron, the ability of MRI to specifically detect cardiac iron is vitally important. Because of these properties, MRI is a valuable modality in determining the degree of cardiac iron overload and monitoring the response to therapy.

R3

USE OF DUAL-ENERGY X-RAY ABSORPTIOMETRY IN EVALUATING TWO FIXATION TECHNIQUES IN KOTZ PROSTHESES. F. Lan*, E. Cohen, R. Bell, J. Kirsh. Departments of Radiology and Orthopedic Surgery, Mount Sinai Hospital, Toronto, Ontario M5G 1X5.

OBJECTIVE. A Kotz prosthesis is utilized in limb salvage procedures for bone sarcoma resection. Fixation has been performed with and without use of screws. Concern has been raised regarding altered stress shielding in patients with screw fixation. Dual-energy x-ray absorptiometry (DEXA) techniques were proposed to evaluate this observation.

SUBJECTS AND METHODS. Twenty patients (6 with screw and 14 without screw) were studied retrospectively using a software modification of the routine DEXA program for hip prosthesis evaluation.

RESULTS. Bone density measurements in each patient were found to be reproducible and technically easy to perform. Although not statistically significant due to the small patient population, there appears to be a difference in native bone densities between the two groups. Progressive loss of bone density distally along the medullary portion of the prosthesis was shown in the group with the screw, as opposed to the non-screw group.

CONCLUSION: DEXA techniques can be applied in the evaluation of patients with Kotz prostheses. Further multi-center and prospective studies will provide large patient populations for further verification of the results.

R4

PREDICTIVE VALUE OF COMPUTED-TOMOGRAPHY (CT) MYELOGRAPHY IN OBSTETRICAL BRACHIAL PLEXUS INJURIES. B. Chow,* H.M. Clarke M.D. Ph.D.,[+] S. Blaser M.D.[++] Division of Plastic Surgery,[+] Department of Radiology,[++] The Hospital For Sick Children, Toronto, ON M5G 1X8.

Introduction: Preoperative radiological studies to detect root avulsions due to birth trauma of the brachial plexus are considered useful in assisting with surgical planning for brachial plexus reconstruction. The presence on CT myelograms of (1) pseudomeningoceles (PM) and (2) PM with the absence of rootlets have been suggested as predictors of root avulsions.

Purpose: The purpose of this study is to investigate the predictive value of PM and PM with absent rootlets in detecting root avulsions determined at time of surgery in infants with obstetrical brachial plexus palsies.

Methods: Forty-four patients with obstetrical brachial plexopathy who have had both preoperative CT myelography and reconstructive surgery at our centre between January 1991 and September 1995 were selected for this study. All CT myelograms were analyzed by a single neuroradiologist blinded to the surgical findings. At each root level of the brachial plexus (C5-T1), the presence or absence of a PM was noted along with the presence or absence of rootlets within each identified PM. Root avulsions were determined from review of operative notes and diagrams by a single investigator blinded to the radiographic results. The operative findings were then compared to the CT myelogram at each corresponding root level.

Results: A total of 220 roots were examined. Twenty-six root avulsions, 42 PM, and 11 PM with absent rootlets were identified. The sensitivity, specificity, positive predictive value and negative predictive value were calculated:

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Val.
Pseudomeningoceles	0.65	0.87	0.41	0.95
PM with absent rootlets	0.35	0.99	0.82	0.92

Conclusion: Given a positive CT myelogram, determing the absence of rootlets in a PM was a better predictor of root avulsion than PM overall. However, PM with or without rootlets are not sensitive indicators of root avulsions. Root avulsion may be ruled out in the absent of a PM on the CT myelogram due to a high negative predictive value.

R5

DETECTION AND STAGING OF PATELLOFEMORAL DISORDERS OF THE KNEE: ASSESSMENT WITH MRI. P. Zia*, C. Hutchison, L. White. Division of Orthopedic Surgery, Mount Sinai Hospital, Department of Surgery, University of Toronto, Toronto, On.

Patellofemoral joint problems are one of the most common presenting complaints in orthopaedic and sports medicine. Although MRI has proven to be extremely useful for evaluating moderately or advanced patellar cartilage injury, conventional MRI has shown to be relatively insensitive to the early changes of chondromalacia patellae.

This study was undertaken to address inter-observer variation in the interpretation of MRIs of the patellofemoral joint. This study also correlated the findings on MRI to those on arthroscopy to delineate the sensitivity and specificity of MRI in the diagnosis of parameters specific to patellofemoral disease.

MR images of knees in 20 patients with various complaints of knee symptoms were retrospectively examined. MR imaging was done with a 1.5-T magnet. T1-weighted axial, coronal, and sagittal images of the knees were reviewed. All MR images were interpreted by 2 independent radiologists blinded to patient identification, previous MR interpretations, and arthroscopic findings. Observers evaluated the images for the presence of an effusion, the patellar fat pad, patellar subluxation, and patellar tilt. They were also asked to evaluate the patellar tendon length and the trochlear angle. Chondromalacia patellae was graded using a modified version of the classification presented by Shahriaree: MR grade 0, normal; MR grade 2, early chondromalacia; MR grade 3, advanced chondromalacia. Arthroscopy of the knee was performed on patients by the same surgeon using a 30-degree Wolff arthroscope and standard three-portal technique. Arthroscopic evaluation of the patella and its surrounding structures was determined by the surgeon who had knowledge of the MRI results. Decision to proceed with arthroscopy was primarily based on patient factors with MRI results having a contributory role Inter-observer reliability of MRI interpretations of the patellofemoral joint was determined. Sensitivity, specificity, and accuracy of MRI in diagnosing patellofemoral joint anomalies were calculated.

Preliminary analysis of results suggest that T1-weighted images have a lower sensitivity, specificity, and accuracy for diagnosing patellofemoral disease than fat-suppressed MRI, and hence a lower inter-observer reliability. In light of the potential clinical utility of MRI, further studies in this area are warranted to define the relative sensitivity, specificity, accuracy, and inter-observer variation of fat-suppressed MRI in the diagnosis of patellofemoral disease.

S1

DEVELOPING A DATABASE FOR EVALUATION OF OUTCOME FROM FACIAL REANIMATION SURGERY. J.M. Burstein*, A.R. Harrop, R.M. Zuker
Division of Plastic Surgery, Hospital for Sick Children, Toronto, Ontario, Canada M5G 1X8

Free muscle transfer for children with facial paralysis has been performed at the Hospital for Sick Children for more than 10 years and surgeons, therapists, and patients, will attest to the operation's success in improving facial animation. To date, however, the quantification of these results has been limited, primarily focusing on technical outcomes of the surgery with less emphasis on patient satisfaction and an integrated rehabilitation team assessment. In the face of shrinking health care resources, greater emphasis is now being placed on global assessment of surgical outcomes. The goal of this project was therefore to develop a database for standardized prospective evaluation of outcome of facial reanimation by free muscle transfer.

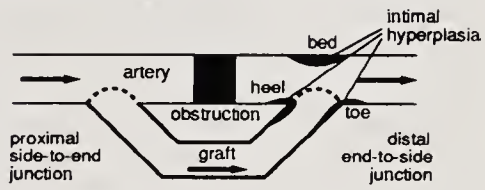
To develop the database input was sought from the various health care professionals participating in the care of these patients: staff surgeons, fellows, occupational therapists, physiotherapists, speech therapists, nurses, and psychiatrists. The recommendations of these individuals were assimilated into a database which will allow standardized pre-operative and post-operative evaluation of the patient. Parameters to be evaluated include: measurements of muscle excursion, smile analysis, speech assessment, patient satisfaction, and overall patient self-esteem. The data base aims to remove subjective interpretation by clinicians or therapists by incorporating the patient's evaluation of the success of the procedure where possible.

The database should serve as an effective tool in the prospective analysis of children with facial paralysis who receive a muscle transfer. By combining the efforts of many disciplines and considering the patient from a broader perspective, the database should accurately help measure the efficacy of free muscle transfer in children who suffer from facial paralysis.

S2

MECHANICAL STRESSES MAY PROMOTE INTIMAL HYPERPLASIA AT GRAFT-ARTERY ANASTOMOSES
P.D. Ballyk[1,2]*, C. Walsh[3] and M. Ojha[1,2], Faculty of Medicine[1], Institute of Biomedical Engineering[2] and Institute of Aerospace Studies[3], University of Toronto, Toronto, Canada, M5S 1A4

Many vascular bypass grafts become obstructed several years post-operatively due to intimal hyperplasia at the distal graft-artery anastomosis. Intimal hyperplasia is an abnormal vessel thickening characterized by the migration of smooth muscle cells from the media to the intima where they proliferate and deposit extracellular matrix. The thickening usually develops around the suture-line and along the bed of the junction, as shown in the figure below, and eventually results in a blood-flow-limiting stenosis.



Experimental evidence suggests that intimal hyperplasia is promoted by either the hemodynamics or structural mechanics at the graft-artery junction. In the present study, we tested the hypothesis that suture-line intimal hyperplasia is part of a remodelling process which reduces the intramural stresses at the junction to a more physiological level.

A novel numerical model of the vascular wall was developed to obtain the stress distributions in (i) a normal artery-artery junction (baseline), (ii) a graft-artery junction *without* intimal hyperplasia and (iii) a graft-artery junction *with* suture-line intimal hyperplasia. The new model outperforms commercial software packages under the large strain conditions expected in the human vasculature.

In the hyperplasia-free simulation, the maximum mean stress was 1.5 times greater than the maximum stress found in the baseline case. In the graft-artery model with suture-line hyperplasia, this maximum stress value was reduced to 1.2 times the maximum baseline value. These results support the hypothesis that the development of suture-line intimal hyperplasia may be part of a remodelling response designed to reduce intramural stresses at the graft-artery junction.

S3

PHAGOCYTE OXIDATIVE BURST IS PRIMED WITH RUPTURE OF AN ABDOMINAL AORTIC ANEURYSM. A. Ghanekar*, T.F. Lindsay. Division of Vascular Surgery, The Toronto Hospital, University of Toronto, Ontario, M5G 2C4.

The mortality rate for patients with ruptured abdominal aortic aneurysm (RAAA) is 50-70%, compared to 3-5% for elective AAA repair. Multiple organ dysfunction (MOD) that occurs after RAAA is a significant cause of mortality. It is hypothesized that RAAA is a form of whole body ischemia-reperfusion that contributes to the activation of circulating phagocytes, initiating a systemic inflammatory state that may result in MOD. Phagocyte oxidant production is a reflection of inflammatory activity, and can be quantitated by measurement of whole blood chemiluminescence (CL).

The hypothesis was evaluated by analysis of CL data previously collected from 22 elective and 15 ruptured AAA patients, and by collection and analysis of perioperative clinical data for each patient. The CL data was generated by measuring unstimulated and stimulated whole blood CL of samples harvested from patients pre-operatively, intra-operatively, and post-operatively for five days. Stimulants used included unopsonized zymosan (UnopZ) and maximal-dose phorbol myristate acetate (PMA).

Non-parametric statistics reveal that phagocyte number is significantly elevated in ruptured patients when they arrive at hospital as compared with elective patients. UnopZ-stimulated CL is increased three-fold in ruptured patients pre-operatively and for the duration of the observational period. PMA-stimulated CL in ruptured patients is significantly increased pre-operatively until the fourth post-operative day. RAAA patients demonstrate lower pre-induction systolic blood pressure, greater frequency of post-operative complications, and longer post-operative ICU stay. One-third of RAAA patients developed complications involving more than one organ system. Three deaths occurred, all among the RAAA group.

We conclude that RAAA causes priming of phagocytes, rendering them capable of increased oxidant production when stimulated; this is associated with increased post-operative complications. Elucidation of mechanisms of priming and types of injury that activate primed phagocytes to initiate systemic inflammation may hasten progress towards therapeutic interventions that decrease morbidity and mortality among ruptured abdominal aortic aneurysm patients.

S4

DISLOCATIONS FOLLOWING TOTAL HIP REVISION WITH ALLOGRAFT. K.P. Panagiotopoulos* and R.D. Masnyk*, P. Ko, Z. Agnidis and A.E. Gross. Division of Orthopaedic Surgery, Mount Sinai Hospital, University of Toronto, Toronto, Canada.

This study evaluated the demographic and surgical variables, as well as risk factors associated with dislocation following total hip revision with allograft.

A retrospective chart review was conducted of 331 patients who had undergone 417 hip revisions with allograft by a single surgeon between 1982 and August, 1995. The variables assessed were: underlying pathology, number of previous hip operations, type of revision prior to dislocation, type of allograft, time to dislocation after revision and the mode of treatment (i.e. closed/open reduction, re-revision or excision arthroplasty).

Forty-three (10.3%) of 417 revisions resulted in 56 total dislocations, forty (71.4%) of which were late dislocations (i.e. at least six weeks post-operatively). Patients having only the acetabular component revised were more prone to dislocation ($p<0.0001$), as were patients with four or more previous operations ($p<0.0001$). There were no apparent relationships with respect to underlying pathology, site of allograft or use of a roof reinforcement ring. Forty-two percent of dislocations ultimately required re-revision following unsuccessful closed reduction.

There is a higher incidence of dislocation in patients who have had four or more previous operations. Revising only the acetabular component is also a significant risk factor for dislocation. Therefore, precautionary measures should be taken within these sub-groups of patients.

S5

IS 95% PANCREATECTOMY THE PROCEDURE OF CHOICE FOR THE TREATMENT OF PERSISTENT HYPERINSULINEMIC HYPOGLYCEMIA OF THE NEONATE? S.J. Fisher*, J. Shilyansky, E. Cutz, K. Perlman, R.M. Filler
Depts. of Surgery, Pathology, and Endocrinology, The Hospital for Sick Children.

Since lesser pancreatic resections failed to prevent hypoglycemia for the treatment of persistent hyperinsulinemic hypoglycemia of the neonate (PHHN, Nesidioblastosis), a 95% pancreatectomy has become the treatment of choice at our institution. We reviewed out experience with regards to the efficacy and long-term consequences of this procedure. Since 1971, 27 infants underwent 95% pancreatectomy for the treatment of PHHN. These children had failed medical management (glucose infusion, glucagon, octreotide, diazoxide) and 85% pancreatectomy in 2. The pancreas was resected leaving only a small part of the gland lying between the common bile duct (CBD) and the duodenum. Follow up ranged from 0.5 to 18 years (mean 8 years). All children became hyperglycemic immediately following pancreatic resection, however hypoglycemia recurred in nine (33%), all within 72 hours. Seven of these were subsequently cured with "near total" pancreatic resection. In 2, hypoglycemia was controlled with diazoxide and frequent feeding because reoperation was refused. Gross anatomical findings and histopathology (islet cell dysplasia 25; nuclear hypertrophy 20; focal adenomatosis 8; diffuse adenomatosis 2) were not predictive of treatment failure. Partial pancreatic regrowth was evident at reoperation in all cases. Following 95% pancreatectomy, 4 of 27 (15%) sustained 5 complications, including one CBD injury. After "near total" pancreatectomy, 3 of 7 children (43%) sustained 4 complications, including CBD injury and mesenteric thrombosis in one. To date, diabetes has developed in 14 children (52%), 8 of 20 after 95% pancreatectomy (at a mean age of 11.6 years) and 6 of 7 after "near total" pancreatectomy (at a mean age of 1.7 years). Diabetes developed in 8 of the 12 children that have been followed for greater than 10 years after 95% pancreatectomy. We conclude that the failure of 95% pancreatectomy to prevent hypoglycemia in one-third of children with persistent hyperinsulinemic hypoglycemia of the neonate and the ultimate development of diabetes in at least two-thirds of them indicates that an alternative treatment strategy is needed.

AUTHOR INDEX

	Abstract	Page
Ahmad, Kamran	PH4	S22
Armour, Alexis	N6	S16
Ballyk, Peter	S2	S25
Banerjee, Probuddha Joy	N1	S15
Barker, Kimberly	PH2	S21
Bender, Jennifer	OB1	S17
Boule, Christopher	C1	S10
Burstein, Jason	S1	S25
Cherry, Nicole	ON6	S19
Chow, Barry	R4	S24
Chu, Eric	B7	S10
Dong, Sandy	CO3	S12
Erb, Grace	OB3	S17
Fisher, Simon	S5	S26
Ghanekar, Anand	S3	S25
Giancola, S. B.	N5	S16
Gorman, Daniel	ON9	S20
Gronau, Karen	ON2	S18
Harris, William	E2	S13
Hartleib, Michael	OP2	S20
Heiber, Michael	B8	S10
Hwang, David	B5	S9
Korman, Mark	ON4	S18
Lan, Frederick	R3	S24
Landolt-Martincorena, Carolina	B2	S8
Lee, Colin	CO1	S11
Li, Madeline	ON7	S19
Liu, David	PS3	S23
Lovinsky, Reena	E3	S14
McCormick, Brendan	B1	S8
Mark, Trisha	ON8	S19
Mason, Cathy	B6	S9
Mehta, Amit	ON3	S18
Milankov, Kosta	ON5	S19
Mostachfi, Omid	N2	S15
Moussadji, Jack	C2	S10
Neogi, Tuhina	B4	S9
Orlean, Alice	PS2	S22
Ossip, Marc	R1	S23
Panagiotopoulos, Kostas	S4	S25
Perelman, Seva	E5	S14
Pressacco, Josephine	ON1	S18
Ransom, Thomas	D1	S12
Sarabia, V.	E6	S14
Sarjeant, Jennifer	PH1	S21
Schumacher, Paul	N4	S16
Sheth, Tarang	CO2	S11
Sheth, Tej	R2	S23
Silverberg, Miriam	PS1	S22
Silverman, Jeffrey	PH3	S22
Somani, Ally-Khan	B3	S9
Somani, Sohel	OP1	S20
Tan, Brenda	OB2	S17
Tsai, Olivia	A1	S8
Verma, Atul	C3	S11
Vohra, Geeta	E4	S14
Walsh, Mark	H2	S15
Wen, Joseph	N3	S16
Wilcox, Bradley	D3	S13
Wojcik, John	H1	S15
Wong, Natalie	P1	S21
Zahariadis, George	E1	S13
Zia, Peter	R5	S24
Znajda, Tamara	D2	S12

SUBJECT INDEX

	Abstract	Page
ANATOMY AND CELL BIOLOGY		
Tsai, Olivia	A1	S8
BIOCHEMISTRY		
McCormick, Brendan	B1	S8
Landolt-Martincorena, Carolina	B2	S8
Somani, Ally-Khan	B3	S9
Neogi, Tuhina	B4	S9
Hwang, David	B5	S9
Mason, Cathy	B6	S9
Chu, Eric	B7	S10
Heiber, Michael	B8	S10
CARDIOLOGY		
Boule, Christopher	C1	S10
Moussadji, Jack	C2	S10
Verma, Atul	C3	S11
COMMUNITY MEDICINE AND EPIDIMEOLOGY		
Lee, Colin	CO1	S11
Sheth, Tarang	CO2	S11
Dong, Sandy	CO3	S12
DIET AND NUTRITION		
Ransom, Thomas	D1	S12
Znajda, Tamara	D2	S12
Wilcox, Bradley	D3	S13
MEDICAL EDUCATION AND PUBLIC HEALTH		
Zahariadis, George	E1	S13
Harris, William	E2	S13
Lovinsky, Reena	E3	S14
Vohra, Geeta	E4	S14
Perelman, Seva	E5	S14
Sarabia, V.	E6	S14
HAEMATOLOGY		
Wojcik, John	H1	S15
Walsh, Mark	H2	S15
NEUROLOGY AND NEUROSCIENCE		
Banerjee, Probuddha Joy	N1	S15
Mostachfi, Omid	N2	S15
Wen, Joseph	N3	S16
Schumacher, Paul	N4	S16
Giancola, S. B.	N5	S16
Armour, Alexis	N6	S16
OBSTETRICS AND GYNAECOLOGY		
Bender, Jennifer	OB1	S17
Tan, Brenda	OB2	S17
Erb, Grace	OB3	S17
ONCOLOGY		
Pressacco, Josephine	ON1	S18
Gronau, Karen	ON2	S18
Mehta, Amit	ON3	S18
Korman, Mark	ON4	S18
Milankov, Kosta	ON5	S19
Cherry, Nicole	ON6	S19
Li, Madeline	ON7	S19
Mark, Trisha	ON8	S19
Gorman, Daniel	ON9	S20
OPHTHALMOLOGY		
Somani, Sohel	OP1	S20
Hartleib, Michael	OP2	S20
PAEDIATRICS		
Wong, Natalie	P1	S21
PHARMACOLOGY AND PHYSIOLOGY		
Sarjeant, Jennifer	PH1	S21
Barker, Kimberly	PH2	S21
Silverman, Jeffrey	PH3	S22
Ahmad, Kamran	PH4	S22
PSYCHOLOGY AND PSYCHIATRY		
Silverberg, Miriam	PS1	S22
Orlean, Alice	PS2	S22
Liu, David	PS3	S23
RADIOLOGY AND MEDICAL IMAGING		
Ossip, Marc	R1	S23
Sheth, Tej	R2	S23
Lan, Frederick	R3	S24
Chow, Barry	R4	S24
Zia, Peter	R5	S24
SURGERY		
Burstein, Jason	S1	S25
Ballyk, Peter	S2	S25
Ghanekar, Anand	S3	S25
Panagiotopoulos, Kostas	S4	S25
Fisher, Simon	S5	S26

University of Toronto

Medical Student Research Day

YOUR PASSPORT TO PRIZES

INSTRUCTIONS: Please detach this form and use it as your personal passport to fabulous prizes. When you visit the various posters on display, simply fill out the **abstract number** of the poster visited and have it **signed** by the presenter of the poster. Once your passport is completely filled out enter it in the **Medical Student Research Day Raffle** to be held at the end of the day! We hope that you will support your colleagues on this day and good luck in the draw.

	ABSTRACT NUMBER	SIGNATURE OF AUTHORIZATION
1		
2		
3		
4		
5		
6		

Your Name:	
Address:	
Phone #:	
Med Year:	
Signature:	

GOOD LUCK !!

AKS
1995

Undergraduate Medical Research at the University of Toronto